American Journal of Diseases of Children

VOLUME 32 AUGUST, 1926 NUMBER 2

THE TREATMENT OF NEPHROSIS

OBSERVATIONS ON SEVEN CASES *

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In any disease of obscure etiology, the effect of various therapeutic measures may be of interest theoretically as well as clinically, because response to treatment may give clues to etiologic factors. It is with this in mind that this report of the treatment of nineteen attacks of generalized edema occurring in seven patients with nephrosis is given. The type of nephrosis considered is that characterized by the presence of marked albuminuria, edema and cholesterolemia, and by the absence of hypertension, hematuria and increase of the nitrogenous elements of the blood.

REVIEW OF THE LITERATURE

In the literature of the past ten years, it is not unusual to find reports of cases which have some of the characteristics of nephrosis, but typical cases such as those described by Epstein [1] are seldom found. Only two papers were found which reported more than one or two cases.

Schwarz and Kohn [2] give seventeen cases, none of which were at any time free from albumin, and in all of which the etiology was obscure, and Clausen [3] reports eleven cases, in four of which the patients were apparently cured by treatment of nasal sinus infections, one of whom, probably cured, later died of cardiac disease. Adamson [4] reported the case of a patient apparently cured by the treatment of edema with Southey tubes. Marriott [5] reports the case of a patient who recovered

* Received for publication, May 25, 1926.
* Read before the Chicago Pediatric Society, April 14, 1926.
* From the Children's Memorial Hospital, Chicago, and the Otho S. A. Sprague Memorial Institute Laboratory.

1. Epstein, A. A.: Chronic Parenchymatous Nephritis, Am. J. M. Sc. **154**: 638 (Nov.) 1917; Nature and Treatment of Nephrosis, ibid. **163**:167 (Feb.) 1922.
2. Schwarz, Herman; and Kohn, J. L.: Studies of Nephritis in Children, Am. J. Dis. Child. **24**:125 (Aug.) 1922.
3. Clausen, S. W.: Parenchymatous Nephritis, Am. J. Dis. Child. **29**:587 (May) 1925.
4. Adamson, C.: Hydraemic Nephritis, Brit. M. J. **2**:1162 (Dec. 20) 1924.
5. Marriott, W. McK.: Parenchymatous Nephritis in Children, M. Clin. N. Am. **7**:1413 (March) 1924.

following treatment of sinusitis. De Rezende [6] cites spontaneous cure in one patient after influenzal pneumonia, and quotes a case of Albutt's which was very similar. De Rezende considered the cure due to a foreign protein reaction. Arbuckle [7] reports two cases cured by treatment of sinusitis. Conrad [8] reports improvement in one case with high protein diet. Karacsony [9] reports a cure in one patient following lobar pneumonia, and considers the result due to some effect of the pneumonia on the body cells, such as a nonspecific protein reaction. McCay [10] had a patient who improved on high protein diet. Rockwood and Barrier [11] report two cases, in which the patients were given calcium chloride treatment. In one, it was a complete failure and in the other it was of apparent benefit. Molnar [12] reported four cases in which he used thyroid medication with gratifying results as far as the edema was concerned. The urinary findings did not clear up, however. Bowen and Boothby [13] gave thyroid extract with good results to two patients with myxedema with kidney complications, but report that they considered thyroid medication dangerous from their experience with it in nephritis without clinical hypothyroidism. Epstein [1] reports improvement in the clinical findings when high protein diets were administered, and says that in some cases thyroid medication seemed to help. According to Volhard,[14] decapsulation does no good in nephrosis. Casper [15] reports no cures in a series of fifty decapsulations. Boyd [16] thought he obtained good results from decapsulation in two patients with subacute nephritis, and considers the operation indicated in obstinate, severe conditions in which cardiovascular lesions are not marked. From the histories, these might have been cases of nephrosis.

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6. De Rezende, C.: Treatment of Nephritic Edema, Brazil-med. **33**:329 (Oct.) 1919.

7. Arbuckle, M. F.: Systemic Manifestations of Suppurative Disease in the Paranasal Sinuses, J. A. M. A. **81**:741 (Sept. 1) 1923.

8. Conrad, C. E.: Nephrosis, Case Report, Virginia M. Month. **48**:375 (Oct.) 1921.

9. Karacsony, G. S.: Case of Chronic Parenchymatous Nephritis Recovering After Pneumonia, Klin. Wchnschr. **4**:455 (March 5) 1925.

10. McCay, D.: Interesting Case of Chronic Parenchymatous Nephritis, Indian M. Gaz. **54**:297 (Aug.) 1919.

11. Rockwood, Reed; and Barrier, C. W.: Calcium Treatment for Edema, Arch. Int. Med. **33**:643 (May) 1924.

12. Molnar, B., Jr.: Treatment of Edema with Thyroid Extract, Wien. klin. Wchnschr. **33**:1111 (Dec. 16) 1920.

13. Bowen, B. D., and Boothby, W. M.: Thyroid Medication in Chronic Nephritis, J. Urol. **1**:469 (Oct.) 1917.

14. Volhard, F.: Surgery of Nephritis, Klin. Wchnschr. **4**:145 (Jan. 22) 1925.

15. Casper, L.: Surgery of Nephritis, Med. Klin. **21**:539 (April 10) 1925.

16. Boyd, F. D.: Two Cases of Decapsulation in Subacute Nephritis, Edinburgh M. J. **26**:104 (Feb.) 1921.

From the literature, therefore, one does not get the impression that any form of treatment has been so uniformly successful as to suggest, per se, any one cause for nephrosis.

The cases here reported include all of those observed in the Children's Memorial Hospital since 1921. All of the attacks of edema that have been closely enough followed to be of value, are included. These data may be of especial value, because the treatments given represent a groping after results, rather than an attempt to prove a previously conceived hypothesis.

Before presenting the case histories, it should be remarked that these cases did not run a stationary or slowly progressive course, but that the disease was marked by a succession of exacerbations and remissions. This feature has not been sufficiently emphasized in other case reports. It is for this reason that in this disease, no report of therapy should be considered of much value unless the patient has been under observation for a prolonged period. One is easily led to false conclusions by results observed in any one attack of edema, just as one might be mistaken in ascribing the crisis in pneumonia to any given therapy. Usual, if not constant, improvement should follow the administration of any treatment before it can be considered beneficial, and cure or improvement should constantly follow a given treatment before this result should be used as an argument favoring any theory as to the etiology of the disease.

In the case histories, laboratory data have been omitted to save repetition. All patients showed marked albuminuria and edema, oliguria at times, and the conditions were characterized by the absence of arterial hypertension, hematuria, increase in nitrogenous elements in the blood and positive Wassermann reactions. In four patients in whom the blood was examined for cholesterol, it was markedly increased.

REPORT OF CASES

CASE 1.—S. S., a girl, aged 3 years, first entered the hospital, June 18, 1922, with generalized edema and ascites, which had been noted one week prior to admission. There had been no previous attack. The present attack was preceded by a "cold." The previous history was negative except for measles at 2½ years, and a cough with sore throat three months prior to examination. Physical examination revealed a moderate generalized edema, marked ascites, bilateral pleural effusions, red throat, purulent nasal discharge and a few coarse râles over the chest. Her mentality was clear. The patient recovered rapidly from this attack, but was subsequently observed in the hospital during seven attacks of marked generalized edema. Records of five of these are sufficiently complete to be of value here. Tonsillectomy and adenoidectomy was performed Dec. 20, 1923, and a second adenoidectomy was performed May 16, 1924, at which time pus was aspirated from the left antrum from which a pure culture of *Staphylococcus albus* was grown. After this procedure, the patient was clinically much improved, but returned late in June with marked albuminuria but no edema. On July 8, Dr. Thomas Galloway made openings from the nose into both antrums and drainage

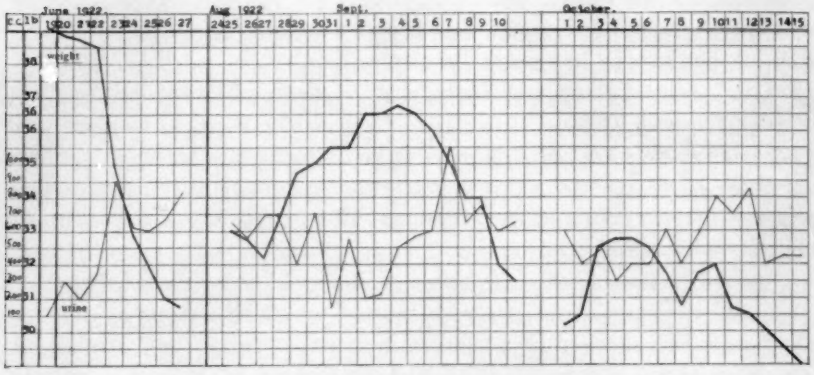


Chart 1 Chart 2 Chart 3

Charts 1, 2 and 3 (case 1).—Treatment: Alkalis, restricted fluids, hot packs and cathartics. Low protein diet in attacks 1 and 2; general diet in attack 3. Infections: Acute coryza with mildly inflamed throat.

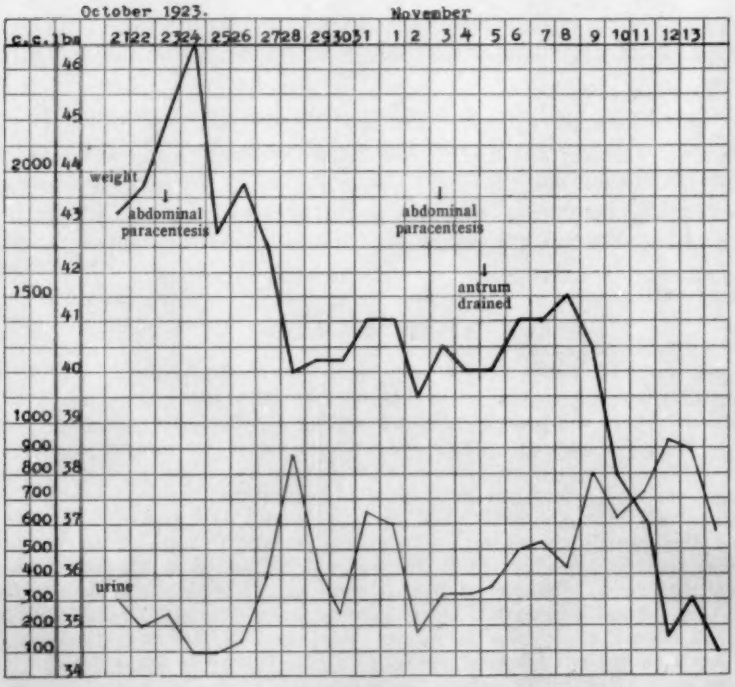


Chart 4 (case 1).—Treatment: Alkalis, restricted fluids, hot packs and cathartics. Low protein diet. Infections: Coryza, pharyngitis, bronchitis and maxillary sinusitis.

was established. The next day and during the ensuing several weeks in the hospital, the urine was negative for albumin. Late in September, the patient was readmitted to the hospital with lobar pneumonia and died in four days without recurrence of edema. Permission for necropsy was denied (charts 1, 2 and 3).

Case 2.—W. B., a boy, aged 4 years, entered the hospital, April 7, 1924, with marked generalized edema and ascites. The attack began four days previously with a "cold," and the edema was not noted until the day prior to admission. Urination was scanty. There had previously been three attacks of edema, one at the age of 1 week, from which the child recovered in three weeks, and two during the preceding year, following "colds." The previous history, in addition, revealed a convulsive attack without edema at 3 months, measles at 2½ years, and frequent "colds." Besides the generalized edema and ascites, physical examination

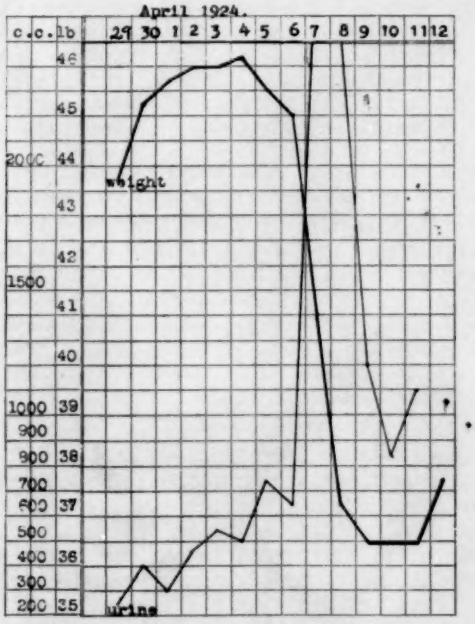


Chart 5 (case 1).—Treatment: Alkalis, restricted fluids, hot packs and cathartics. Low protein diet. Infections: Acute coryza, maxillary sinusitis.

showed tonsillitis, bilateral otitis media requiring paracentesis, moderate cervical adenitis and a purulent nasal discharge. The boy rapidly improved after the paracentesis, but had a recurrence of edema within two weeks. This again promptly subsided after opening the ear. The palpable edema entirely disappeared, but a small amount of fluid remained in the abdomen and the patient continued to appear puffy. The intradermal salt solution test[17] showed a shortened disappearance time (about from twenty to thirty minutes), indicating, we think, an increased affinity of the tissues for water. The albuminuria was constant during his stay in the hospital. At irregular intervals, coincident with upper respiratory infections, the boy would suddenly develop edema, as illustrated in chart 15. The tonsils and adenoids were removed May 22, at which time pus was aspirated from

17. McClure, W. B., and Aldrich, C. A.: Time Required for the Disappearance of Intradermally Injected Salt Solution, J. A. M. A. **81**:293 (July 28) 1923.

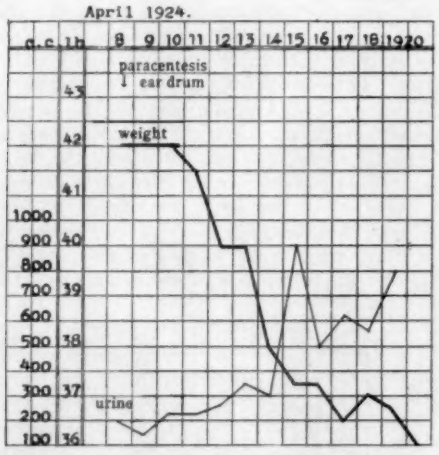


Chart 6 (case 2).—Treatment: Alkalis and hot packs. Low protein diet. Ten grains of theobromin sodiosalicylate were given three times daily from April 8 to 11. Infections: Rhinitis, tonsillitis, moderate cervical adenitis.

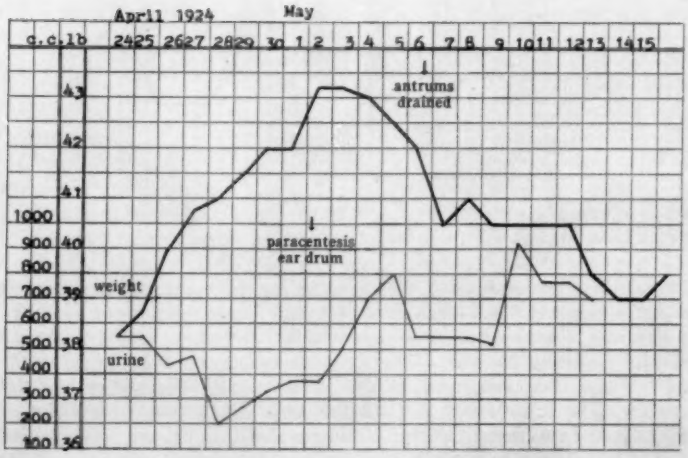


Chart 7 (case 2).—Treatment: Alkalis until May 5, cathartics and low protein diet. Five grains of theobromin sodiosalicylate were given three times daily. Infections: Maxillary sinusitis, otitis media, moderate tonsillitis and cervical adenitis.

the left antrum which produced *Staphylococcus albus* in pure culture. As no improvement followed, on July 28 openings were made from the nose into both antrums. To our disappointment the patient did not improve. Various attempts were made to clear up the chronic nasal infection; these consisted of local applications, nasal suction, autogenous vaccine and milk injections. The symptoms persisted, and the patient was discharged March 22, 1925, improved but not cured. We have been unable to trace him since that time (charts 4 and 5).

CASE 3.—V. C., a boy, aged 8 years, entered the hospital, Aug. 7, 1923, with generalized edema which had been gradually increasing for three weeks. There had been no preceding "cold." The previous history was negative except for

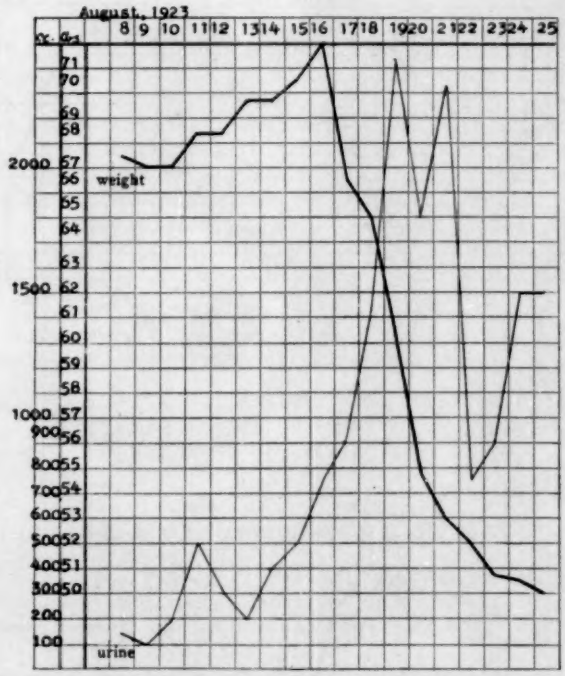


Chart 8 (case 3).—Treatment: Alkalis, restricted fluids, hot packs and cathartics. Low protein diet. Infections: Inflamed throat.

measles and occasional sore throats. Physical examination revealed generalized edema, ascites, bilateral pleural effusions, carious teeth, reddened tonsils and nasal and pharyngeal membranes. This attack cleared up promptly, but the albuminuria persisted. After almost two months of hospitalization, the boy again began to swell up. October 15, tonsils and adenoids were removed under ether anesthesia. Soon after this, an erysipelas-like red swelling appeared in the lower left eyelid. This gradually localized into an abscess, which was incised and drained October 25. Streptococci were obtained in pure culture from this pus. In about five days all edema was gone. The albumin gradually disappeared from the urine, and the boy has been well since that time. It was the opinion of the rhinologist consulted that the abscess resulted from an ethmoid sinusitis (charts 6 and 7).

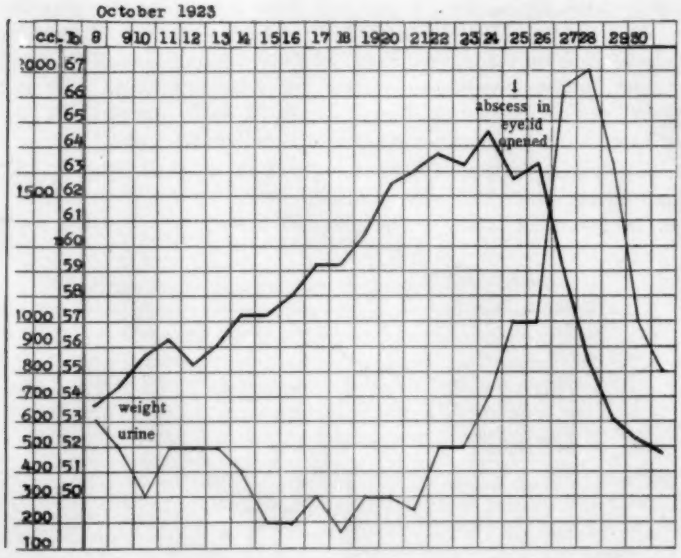


Chart 9 (case 3).—Treatment: Alkalis, restricted fluids, hot packs and cathartics. Low protein diet. After October 18, 7.5 grains theobromin sodio-salicylate were given every three hours. Infections: Ethmoid sinusitis rupturing through the orbit.

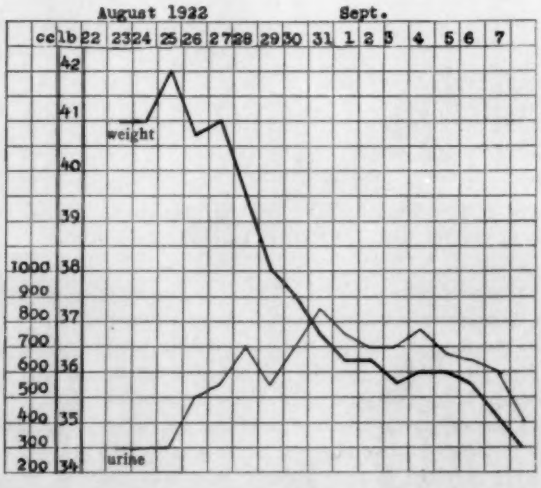


Chart 10 (case 4).—Treatment: Restricted fluids, alkalis, hot packs. Low protein diet. Infections: Coryza and pharyngitis.

CASE 4.—J. G., a boy, aged 3 years, entered the hospital, Aug. 21, 1922, with generalized edema and ascites which had been present for two weeks. The previous history was negative except for measles at 2 years. Physical examination revealed the anasarca, an infected throat and nasal discharge. The edema gradually subsided in two weeks, and on September 20 he had a very slight return of edema associated with a "cold." Soon after, however, the family left the city and the patient has not been seen since (chart 8).

CASE 5.—M. R., a girl, aged 5 years, entered the hospital, Feb. 17, 1925, because of generalized edema of mild degree. Swelling of the face, associated with "bronchial colds," had appeared at frequent intervals during the past five months. There was a previous history of mumps and frequent "colds." Besides the generalized edema, physical examination revealed hypertrophied tonsils, slight cervical adenopathy, a functional systolic heart murmur and the coarse râles over the chest. The antrums did not light up well on transillumination, and pus exuded

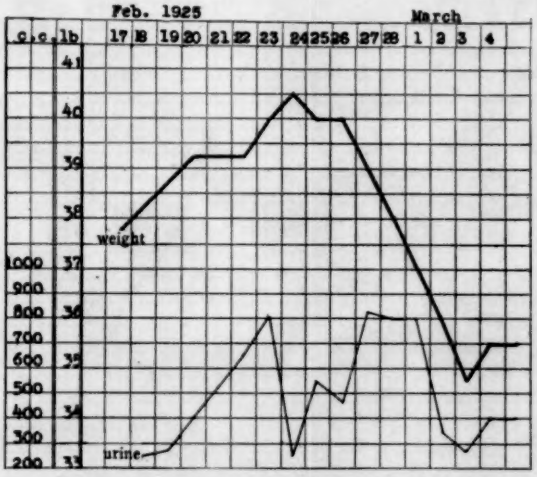


Chart 11 (case 5).—Treatment: General diet and fluids liberally. Infections: Maxillary sinusitis, otitis media, pharyngitis, asthmatic bronchitis. Tonsils and adenoids were removed and antrums punctured subsequent to this attack.

from the right nares with suction. The right malar bone was somewhat tender, and the ear-drums were pink. This attack was of moderate severity and subsided so that the edema was all gone on March 5. On March 2, the tonsils and adenoids were removed. At this time, the right antrum was punctured and pus was obtained from which *Staphylococcus albus* was cultured. About March 18, the patient again began to have edema, coincident with a definite, mild upper respiratory infection. The edema increased very rapidly About March 24, she contracted an acute sore throat from the patient in the next bed, had an elevation of temperature of over 105 F., developed edema of the soft palate, erysipelas-like swelling about, first, the left, and then the right eye, an acute otitis media, bronchitis, and finally a metastatic abscess in the region of the right greater trochanter. The edema began to subside in about two days after the onset of this streptococcal throat infection, and completely disappeared during the course of the high septic temperature. The eyes discharged staphylococcus pus, but as the drainage was deemed insufficient, incisions were made in both lower eyelids on April 4, and the left ear-drum was incised, the pus culturing stapyhlococcus.

On April 21, it was discovered that there was a septal abscess in the nose which communicated with the discharging incisions in the eyelids, and this abscess was drained. On May 3, the abscess on the right hip was opened, a pure culture of hemolytic streptococci being obtained. After the disappearance of the edema, and while the temperature was still elevated, about two weeks after the onset of the streptococcus infection, the urine showed blood macroscopically, many casts, and in spite of this, distinctly less albumin. After the hip drainage the patient made an uneventful recovery, and was discharged July 7 after having been free from albumin for some time. The patient has since been observed at frequent intervals, and has had no recurrence either of edema or albuminuria. This history is given in full detail because this patient probably had a chronic nephrosis with an acute

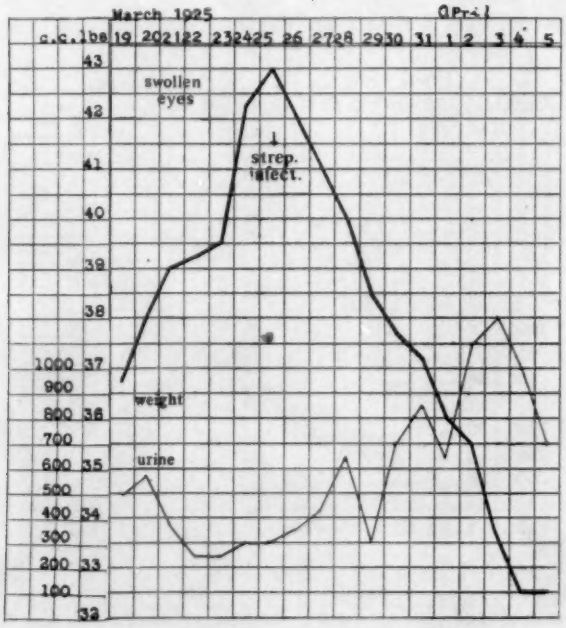


Chart 12 (case 5).—Treatment: Full diet and fluids liberally. Thyroid extract until March 20. Infections: Coryza, staphylococcal maxillary sinusitis, septal abscess and abscesses of lower eyelids. Acute streptococcic infection of the throat with otitis media began about March 24.

hemorrhagic nephritis superimposed on it. Coincident with the streptococcal infection and with the localization of the staphylococcal abscesses, the symptoms of the nephrosis subsided. The hemorrhagic nephritis cleared up after all evidence of infection had gone (charts 9 and 10).

CASE 6.—W. M., a boy, aged 7 years, entered the hospital, April 27, 1925, with generalized edema which followed a "cold" three weeks prior to examination. There was a previous history of similar attacks at irregular intervals during the past two years, which were increasing in severity. During these two years the patient had diphtheria and measles, and a tonsillectomy had been performed. Physical examination revealed marked generalized edema, ascites, nasal discharge, inflamed throat, an injected remnant of the right tonsil, slight cervical adenopathy

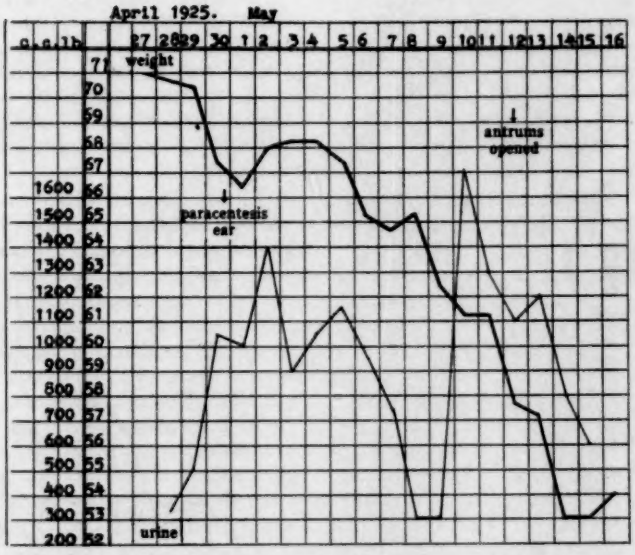


Chart 13 (case 6).—Treatment: Fluids were given liberally and diet was general. Infections: Maxillary sinusitis, pharyngitis and otitis media.

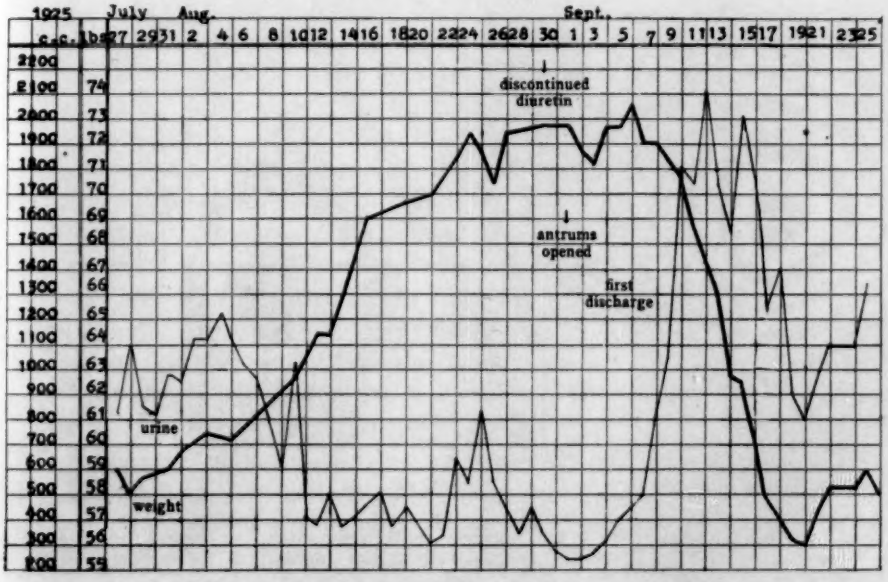

1925 July Aug. Sept.
c.c. lbs
27 29 31 2 4 6 8 10 12 14 16 18 20 22 24 26 28 30 1 3 5 7 9 11 13 15 17 19 21 23 25
discontinued diuretin
antrums opened
first discharge
urine
weight

Chart 14 (case 6).—Treatment: General diet and fluids liberally. Theobromin sodiosalicylate was given until August 29. Infections: Maxillary sinusitis, pharyngitis. Sinus operation September 1.

and an immensely distended scrotum filled with fluid and intestines (bilateral inguinal hernia). On April 30, paracentesis of the left ear-drum was performed and the edema rapidly subsided. As the urinary findings did not improve, on May 12 both antrums were washed out and a pure culture of *Streptococcus hemolyticus* was found. On June 22, the tonsil and adenoid remnants were removed and the sinuses were again punctured. This time the cultures showed *Staphyloccoccus aureus*. The patient had a slight elevation of temperature beginning July 8, and

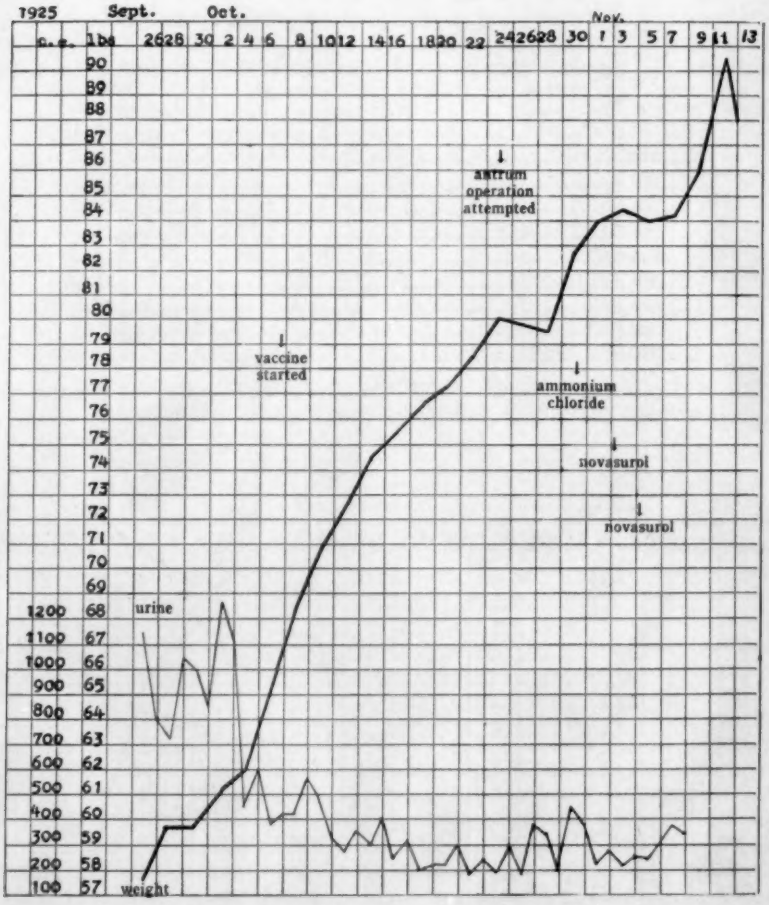


Chart 15 (case 6).—Treatment: General diet and fluid liberally. Autogenous vaccine. Ammonium chloride October 30 to November 3. Merbaphen was given November 2 and 4. Infections: Maxillary sinusitis, pharyngitis, and terminal pneumonia.

a little edema appeared. A few purpuric spots were noted. Marked edema again appeared about August 7. There was a red throat and little nasal discharge. On September 1, at the height of the edema, windows were made from the nose into the antrums. They discharged macroscopic pus on September 5, following which immediate and complete disappearance of the edema occurred. A trace of albumin remained in the urine, however. Almost immediately after the abatement

of the nasal discharge, the edema began again and reached tremendous proportions. Another antral drainage was attempted, but was unsuccessful because of an alarming hemorrhage. Vaccine therapy was tried (autogenous staphylococcus), calcium salts were given, and finally merbaphen was tried, all of which did no good and the last of which, I think, made him definitely more toxic. The patient developed signs of pulmonary infection and on November 13, while a transfusion was being performed, died. Bronchopneumonia was the probable cause of death. Necropsy was not permitted (charts 11, 12 and 13).

CASE 7.—D. K., a girl, aged 5 years, entered the hospital, May 5, 1921, with general anasarca. For about nine months, at irregular intervals, the parents had noted this appearance to a lesser degree. There was a previous history of german measles, pertussis and mild sore throat. Physical examination revealed generalized edema and ascites, enlarged thyroid, carious teeth and sclerosed tonsils. During her stay in the hospital, the bad teeth and tonsils were removed. During this time she has four attacks of marked edema associated with "colds." The urine contained albumin constantly. During the fourth attack she developed severe bronchopneumonia and was taken home against advice. She recovered rapidly, has had no recurrence of albuminuria or edema and has since, in the dispensary, been observed to be perfectly well on several occasions (chart 14).

The accompanying charts show graphically the course of the attacks of edema in these seven patients. The daily weight and urinary output curves are given, with notes as to the treatment being used in each instance. An attempt to summarize the results of the more commonly used methods of treatment follows.

SUMMARY OF RESULTS

Dietary Measures.—Diuresis occurred while low protein diet was being administered in twelve instances (attacks 1, 2, 4, 5, 6, 7, 8, 10, 16, 17, 18 and 19 *), and while high protein diet was being given in six instances (attacks 3, 9, 11, 12, 13 and 14). On the other hand, edema increased for long periods with low protein diet in six instances (attacks 2, 3, 7, 17, 18 and 19), and with high protein diet in five instances (attacks 9, 12, 13, 14 and 15). Because of the negative results so often seen from its use, salt free diet was seldom tried, but in the two instances in which it was used the edema increased during the time of salt restriction. Chart 15 is included to illustrate the fact that various diets had no influence over the wave-like course of the edema in one patient (case 2). The course of the disease is shown in this case over a period of almost six months. Nowhere can one find that change of diet influenced the edema favorably. The fact that no special diet resulted in constant or usual benefit in these cases suggests that dietary measures in this disease are of secondary importance. It is my impression that the children on a diet rich in protein looked and acted better than those who were on a low protein regimen.

* The attack numerals correspond with the chart numerals in each instance.

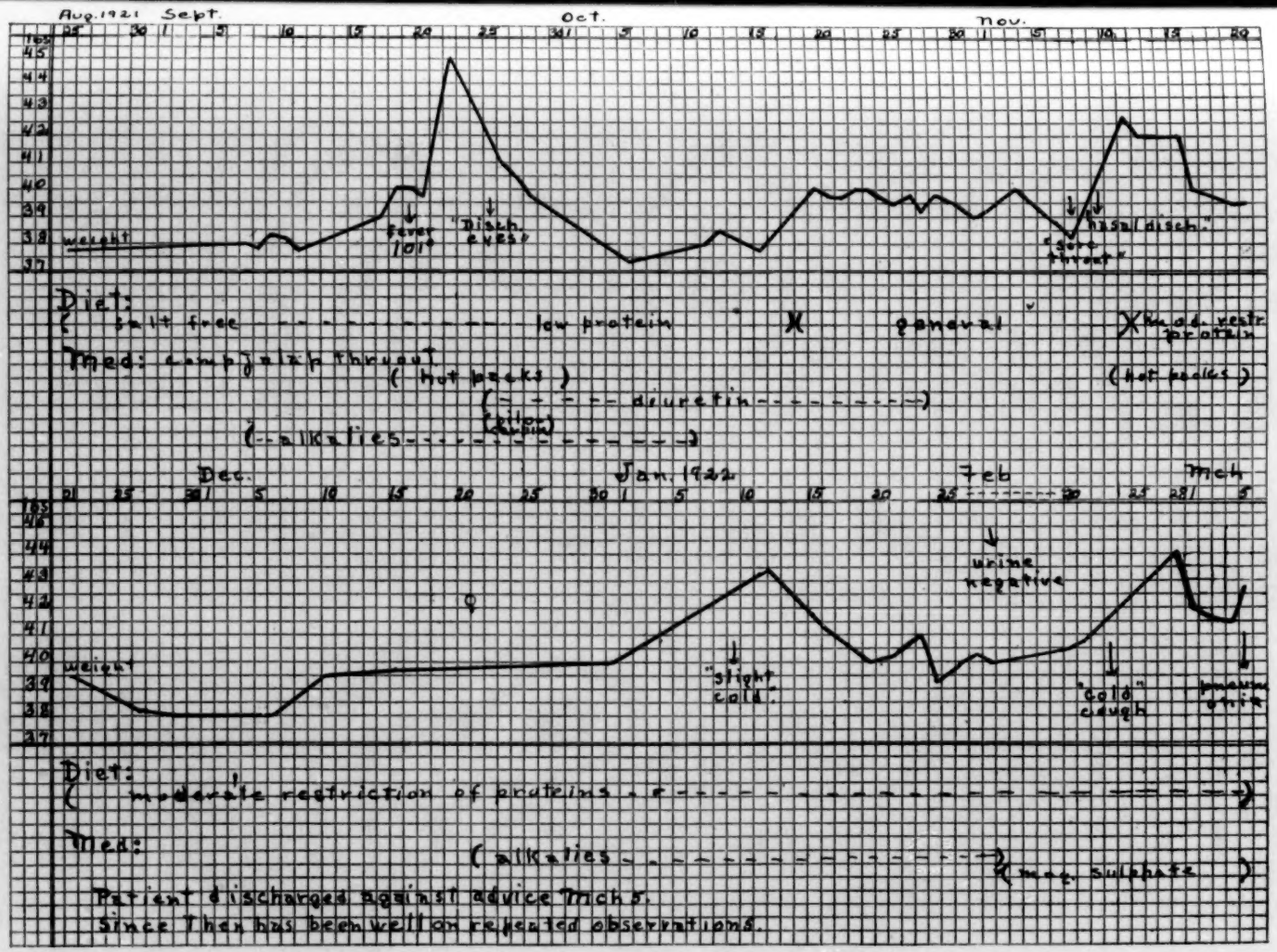
Dehydrating Measures.—Fluid restriction, usually combined with the use of hot packs and cathartics, was tried in twelve instances (attacks 1, 2, 3, 4, 5, 8, 9, 10, 16, 17, 18 and 19), all of which eventually went on to discharge of the edema. In the remaining seven attacks (6, 7, 11, 12, 13, 14 and 15), fluids in abundance were given, or were forced, hot packs were not used, and cathartics were given only as required. The charts show that, except in the last attack of case 6, the latter method seemed to bring about as good results as did attempts at dehydration. Clinically, however, the patients who were allowed water in liberal amounts were much less toxic than those in whom it was restricted. Even with tremendous edema, these patients seldom complained of headache or nausea and were not drowsy. There is a theoretic objection to fluid restriction, which was previously discussed in another paper.[18] It is possible that edema in these cases may be a protective mechanism, acting as a diluent of toxins. Plass and Bogert,[19] speaking of the edema of toxemia of pregnancy, suggest the same possibility. If this is true, the use of dehydrating measures combined with fluid restriction during the stage of increasing edema, might increase the intoxication dangerously. For this reason, and because I have not seen impressive evidence of the value of fluid restriction, it has seemed wise to allow fluids liberally to patients undergoing dehydrating treatment.

Administration of Alkalis.—In twelve instances (attacks 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 16 and 17), alkalis were given in an attempt to alkalinize the urine. They did no apparent harm, as the conditions in which they were not given ran approximately the same sort of course. That they might have been beneficial in the eight attacks in which diuresis occurred under their administration is doubtful, since increase of edema occurred during prolonged alkaline treatment in six instances (attacks 2, 3, 7, 9 and 16 and 18). It is as reasonable to suppose that they caused the increase of edema in these six, as to hold that they decreased it in the twelve.

Theobromin Sodiosalicylate.—This drug was given in five attacks (6, 7, 9, 14 and 16). In two of these (6 and 7), it appears from the charts to have been of possible benefit. In attack 9, however, diuresis was delayed nine days after its first administration; in attack 16 it was first given two days after diuresis had begun, and in attack 14, the patient gained 14¾ pounds (6.6 Kg.) during the thirty days it was given, and lost all the edema immediately after its discontinuance. These results illustrate how careful one must be in ascribing results to

18. Aldrich, C. A.: A Study of the Clinical Course of Generalized Edema, J. A. M. A. **84**:481 (Feb. 14) 1925.

19. Plass, E. D., and Bogert, L. J.: Plasma Protein Variations in Normal and Toxemic Pregnancies, Bull. Johns Hopkins Hosp. **35**:361 (Nov.) 1924.



Charts 16, 17, 18 and 19 (case 7).—Treatments indicated on chart.

therapy on the evidence of isolated cases. Theobromin sodiosalicylate was of no usual or constant benefit.

Tonsillectomy and Adenoidectomy.—This operation was performed on all of these patients, but there is no suggestion in the course of the disease that it influenced in any way their recovery or freedom from subsequent attacks. It is also interesting to note that in none of these cases was there a definite history of acute tonsillitis preceding any attack. The upper respiratory infection accompanying them was not of the acute, fulminating type, it was a mere "cold."

Drainage of Infected Areas.—Although in the preceding methods of treatment, results were decidedly questionable, reference to the charts shows that wherever demonstrable abscess formation took place and was successfully treated, sudden diuresis took place. This happened in seven instances (attacks 4, 6, 7, 9, 12, 13 and 14). Treatment consisted of paracentesis of the eardrum in three subjects; drainage of the antrums in three; incision of abscess from perforating ethmoiditis in one subject, and the localization of a nasal septal abscess and of a subacutaneous abscess in the region of the hip, both in the same case. Disappearance of edema was complete and began immediately in all these instances except one. In the case with incomplete discharge of edema, all pitting edema disappeared, but some fluid remained in the abdomen, and the patient looked puffy throughout a course which we were unable to influence further (case 2). Another patient, after complete discharge of edema following antral drainage, had a recurrence of the edema and eventually died, attempts at reestablishing drainage of the antrum failing because of serious hemorrhage. Since successful drainage of abscesses in the nasal region always resulted in diuresis and disappearance of edema, it is probable that an infection in some way was the cause of the oliguria and edema. It is considered that drainage of infected areas might not be curative unless all the regions so infected could be successfully treated. In these chronic processes of the upper respiratory tract, it is very likely that persistence of infection in unknown, or unreachable locations may account for the recurrences and for the chronicity of the disease.

The fact must not be overlooked, however, that in eleven instances (attacks 1, 2, 3, 5, 8, 10, 11, 16, 17, 18 and 19), disappearance of edema occurred without visible abscess formation or drainage. To my mind, the important point to be observed is that all attacks were associated with infections. Spontaneous recovery from a "cold" should, theoretically, result in the elimination of edema just as readily as abscess drainage had this effect, if we consider that active infection is the cause of the disease. Emphasis is laid on the results from abscess drainage simply because they are more easily demonstrable. One can point to

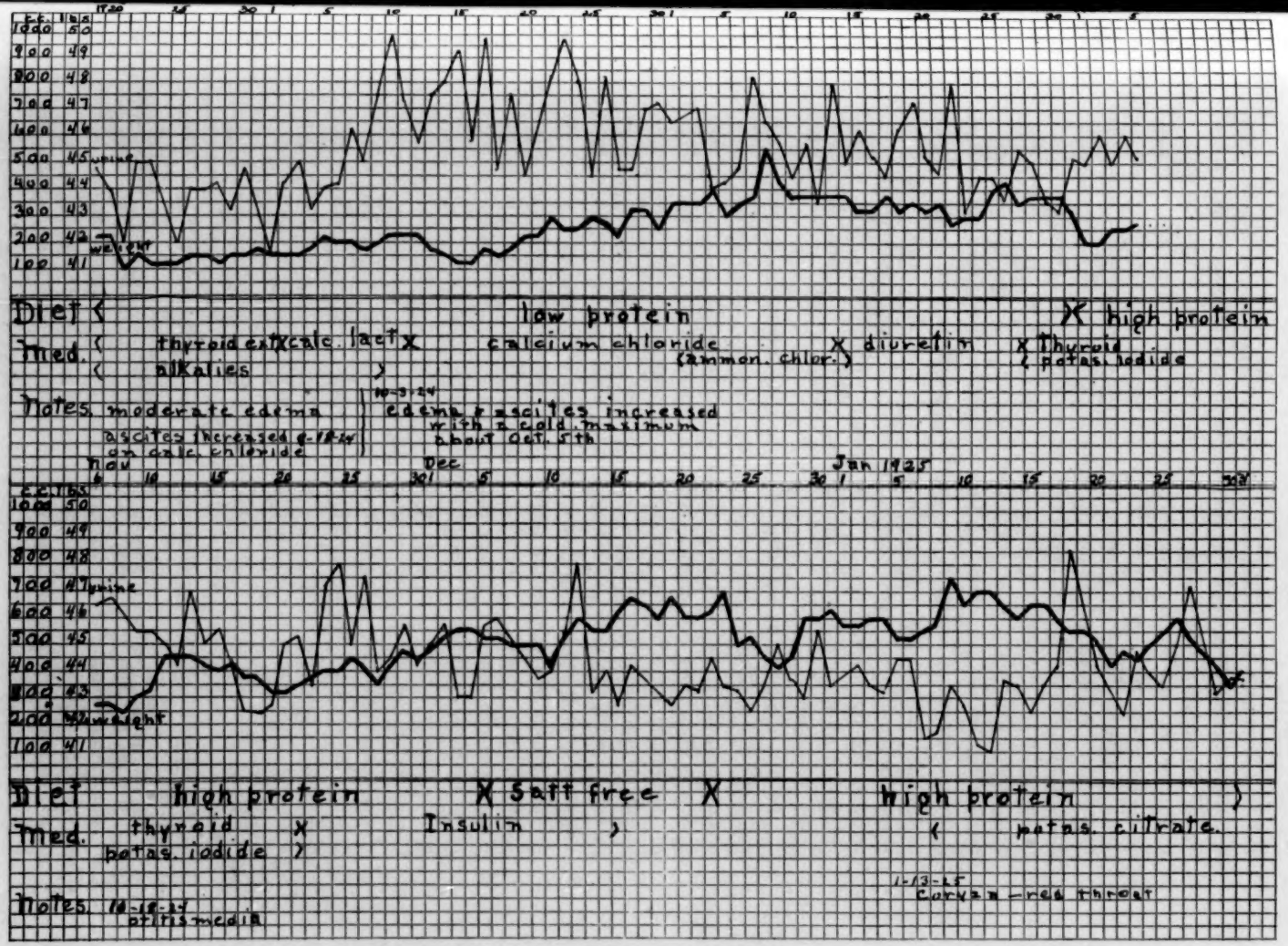


Chart 20 (case 2).—Note the irregular weight curve and the lack of relationship between loss or increase in weight and any of the treatments tried.

the date on which an operation was performed and show the result on a chart, whereas it is clinically impossible to state at just what time a "cold" has begun to improve.

COMMENT

The only method of treatment which can be demonstrated to have produced any constant, temporary or permanent benefit in these cases, is drainage of infected areas, usually in the nasal region. This is in direct accord with the observations of Clausen and Marriott. It is surprising that neither Epstein nor Schwarz and Kohn mention the occurrence of nasal infection in their cases. All the patients we have seen have given definite evidence of infection, and the fact that increase in the symptoms of the nephrosis so frequently coincided with exacerbations of the nasal infection, would be suggestive of a probable etiologic relationship, even without the therapeutic results here shown. This brings us to a consideration of what reasonable deductions as to etiology may be drawn from these data.

To my mind, the promptness of diuresis following abscess drainage rules out the possibility that a renal lesion is primary in this disease. In some cases, after weeks of extreme oliguria, practically perfect function is developed almost over night. It is not consistent with our knowledge of pathologic behavior to suppose that inflammatory or degenerative lesions of long standing can heal so completely in a few hours. This is in accord with the views of many writers who look toward extrarenal factors as the cause of nephrosis. M. H. Fischer [20] maintained that an increase in the water imbibing power of the tissue cells was responsible for the edema. Volhard [21] thought extrarenal factors caused the edema. Kaufmann and Mason [22] believe that nephrosis is an early manifestation of a systemic cellular degeneration of unknown origin. Clausen [23] reports the isolation of a surface tension reducing substance from the blood and urine of patients with nephrosis. This substance he considers responsible for changes in the equilibrium of the normal water balance between the tissues and the body fluids, resulting in edema and abnormal urinary findings. McClure and myself,[24] as a result of work with the intradermal salt solution test, suggested the possibility that a

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20. Fischer, M. H.: Oedema and Nephritis, New York, John Wiley & Sons, 1910.

21. Volhard, F.: Die Doppelseitige Haematogischen Nierenkrankheiten, Berlin, 1918.

22. Kaufmann, Joseph; and Mason, Edward: Nephrosis, a Clinical and Pathological Study, Arch. Int. Med. **35**:561 (May) 1925.

23. Clausen, S. W.: Parenchymatous Nephritis. III. Am. J. Dis. Child. **29**:594 (May) 1925.

24. Aldrich, C. A., and McClure, W. B.: The Intradermal Salt Solution Test II, J. A. M. A. **82**:1425 (May 3) 1924.

toxic substance elaborated in infected areas might so change the affinity of the body cells for water that they would absorb more than normally and so produce edema. Results from treatment in these cases, therefore, indicate that nasal infection in some way causes the symptoms of nephrosis. The promptness of response to abscess drainage makes it seem improbable that a chronic renal lesion is primary, and gives some support to those who explain edema on extrarenal grounds.

While these findings are in general agreement with those of Clausen, it seems to me that he limits the case too closely when he concludes that "the cause of parenchymatous nephritis is nasal sinusitis." In this series, diuresis followed treatment of otitis media, septal abscess and spontaneous recovery from "colds." It would seem more reasonable to assume that an infection of the upper respiratory tract was the cause, and that following this, frequent localization in the nasal sinuses takes place. This localization, no doubt, is a factor in the chronicity of some cases. Clausen also suggests that a specific staphylococcus is an etiologic factor in these infections, although he calls attention to the fact that this organism has not been proved pathogenic. Cultures from these cases were not in strict agreement with his observations, since in three instances streptococci were also found in pure culture from abscesses (cases 3, 5 and 6). Moreover, while it is undoubtedly true that staphylococci are usually cultured from these locations in nephrosis, it is equally true that they are found in practically all of the noses of healthy children, often in pure culture. It would seem that until the staphylococci cultured from these cases are demonstrated to be either pathogenic, or edema producers in experimental animals, very strong evidence as to their relationship must be produced before we can consider that the positive cultures from nephrosis cases are more significant than the positive cultures from the noses of normal children. This is, however, an attractive hypothesis, and efforts are at present being made to demonstrate pathogenicity in the staphylococcus cultured from case 6.

Before leaving the subject of the bacteriology of these infections, another interesting observation should be noted. All three of those patients definitely cured (cases 3, 5 and 7), became well during convalescence from acute infections complicating the nephrosis. In case 3, the condition was streptococcus ethmoiditis; in case 5, streptococcus throat infection with a metastatic abscess was the condition, and in case 7 the condition was bronchopneumonia. The edema actually disappeared while one patient (case 5) was having a high septic temperature from the throat infection, in spite of staphylococcic abscesses in the nose which were not surgically drained until after diuresis. None of these patients has since had return of edema or albuminuria. In explanation of this, three possibilities come to mind: First, pure coincidence; second, a nonspecific protein reaction may have taken place, so

altering the situation that the body was able to overcome the chronic intoxication, and, third, the streptococcus intoxication might have acted as a dehydrating force in opposition to the hydrating force assumed by some to be present in nephrosis. De Rezende, in reporting his subject cured after influenzal pneumonia, goes on to say that he intends to treat his next case of nephrosis with foreign protein, and Marriott,[25] in his paper on the relationship between mastoiditis and intestinal intoxication, speaks of the streptococcus as having an hydrolabile effect on the organism. It is attractive, but must still be speculation, to consider that, in these three instances, a streptococcus intoxication of dehydrating power cured the nephrosis by combating a staphylococcus intoxication of hydrating power.

SUMMARY

1. Results of treatment in nineteen attacks of generalized edema occurring in seven patients with nephrosis are reported.

2. All of these patients had definite nasal infections. Successful drainage of abscesses resulting from these infections gave constant and promptly beneficial results, as illustrated by diuresis.

3. Many attacks subsided with spontaneous improvement in the nasal infection.

4. Administration of alkalis, theobromin sodiosalicylate, various dietary regimens and dehydrating measures, combined with fluid restriction, resulted in no usual or constant improvement in the symptoms.

5. Tonsillectomy and adenoidectomy did not prevent recurrence.

6. All three of the permanently cured patients became well immediately on recovery from acute febrile infections complicating the nephrosis.

545 Lincoln Avenue.

25. Marriott, W. McK.: Further Observations Concerning the Nature of Nutritional Disturbances, abst., Am. J. Dis. Child. **30**:577 (Oct.) 1925.

THE HYDROGEN ION CONCENTRATION OF THE STOOLS OF NEW-BORN INFANTS*

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The present work was undertaken to determine the p_H of the meconium, as compared with that of the stools of normal breast-fed infants; to follow the transition, in case of any significant difference, from the p_H of the meconium to the p_H of the stools after breast milk feeding, and to see whether, under similar conditions, large or slight variations occur in the p_H. An attempt has been made to show the significance of meconium to the metabolism of the new-born infant.

For a long time, it was customary to observe simply whether the stools were acid or alkaline to litmus and other indicators. Breast milk feeding gave acid stools; cow's milk modifications resulted in alkaline stools. Langstein [1] determined the acidity of a number of infants' stools in terms of normal acid or base required for neutralization. The results varied with the indicators used. Titration methods do not, however, show the true acidity. Sörensen, in 1912, and Michaelis, in 1914, proved that true acidity depends on the hydrogen ion concentration. They gave methods of determining accurately the true acidity. Howe and Hawk [2] found by electrometric measurements that the normal C_H of adult human feces falls within the range 9.8×10^{-8} to 0.15×10^{-8} (p_H 7.1 to 8.8). Nelson and Williams,[3] using colorimetric methods, found the usual range to be p_H 5.38 to 6.66. Ylppö [4] determined the p_H of the stools of normal infants; the stools of breast fed infants showed p_H 4.6 to 5.0, and of artificially fed, p_H 7.0 to 8.3. Tisdall and Brown [5] have made

* Received for publication, Jan. 22, 1926.

* From the Department of Pediatrics, Yale University.

* Presented in partial fulfilment of the requirements for M.D. degree, Yale University, July 1925, by R. C. Norton.

1. Langstein, L., quoted by Czerny, A. D., and Keller, A.: Untersuchungen über die acidität und den Zuckergehalt von Säuglingsstühlen, Jahrb. f. Kinderh. **56**: 350, 1902.

2. Howe, P. E., and Hawk, P. B.: Studies on Water Drinking. Fasting Studies. Hydrogen-Ion Concentration of Feces, J. Biol. Chem. **11**:129-140, 1912.

3. Nelson, C. F., and Williams, J. L.: Urinary and Fecal Output of Calcium in Normal Men, with Observations on the p_H of Urine and Feces, J. Biol. Chem. **28**:231-236, 1916.

4. Ylppö, H.: Neugeboren-, Hunger-, und Intoxikations- Acidosis in ihren Beziehungen zueinander, Ztschr. f. Kinderh. **14**:268-448, 1916.

5. Tisdall, F. F., and Brown, A.: Acidity of Infants' Stools, Am. J. Dis.Child. **27**:312-331 (April) 1924.

the most recent p_H determinations. None of these investigators reported the hydrogen ion concentration of meconium.

MATERIAL

Specimens from twenty-seven infants born in the obstetrical pavilion of the New Haven Hospital were obtained through the kindness of Dr. Arthur Morse. The infants were consecutive cases and were breast fed from birth. Babies artificially fed from birth were not included. Twenty-one were exclusively breast fed, six later received supplementary feeding of cow's milk with added carbohydrate. One was a premature infant weighing 1,800 Gm. at birth. The others weighed 2,950 Gm. or more at birth, the average being 3,600 Gm., and all regained their birth weight by the tenth day. Thus the material consisted of normal breast-fed infants.

METHOD

The specimens were most satisfactorily obtained by means of a short, straight piece of glass tubing with smoothed ends. The tube, and a test tube to contain it, were boiled in distilled water, and allowed to drain until dry. This procedure sterilized the tubes, and at the same time minimized the occurrence of traces of acid or basic substances on the glassware which might interfere with the accuracy of the results. By careful insertion of the tube into the infant's rectum, it was nearly always possible to collect a sufficient amount of material in the end of the tube for a p_H determination. The specimens were either examined immediately, that is, within an hour, or put in a refrigerator and examined within twelve hours. The observations of Tisdall and Brown,[5] that the p_H of the stools does not change appreciably within this length of time, were confirmed.

In an effort to obtain a clear and colorless fecal extract suitable for colorimetric determination, the method of filtering, and the method of centrifuging for an hour or more at high speed, were tried. However, dialysis through collodion sacs used by Levy, Rowntree and Marriott for blood, and by Tisdall and Brown [5] for stools, proved simpler, as well as more accurate.

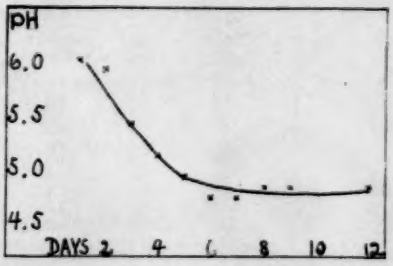
An amount of stool specimen, at least the size of a pea, was mixed with from 10 to 15 parts of freshly boiled distilled water. Inside a large test tube containing this mixture was placed a collodion sac, the size and shape of a smaller test tube. This collodion sac held about 15 cc. of freshly boiled distilled water. Dialysis was allowed to proceed for twenty to thirty minutes, although five minutes is ample time for the fluid in the collodion sac to come to nearly constant p_H. The clear colorless fluid was then removed from the sac, which, after rinsing, could be used for further determinations.

The p_H of the dialysate was then read by colorimetric comparison with standard buffer solutions, made up to known p_H values. The colorimetric method of Clark and Lubs was used, with standard solutions made up at intervals of 0.2 p_H and checked electrometrically. Instead of the relatively unstable methyl red in Clark's [6] series, the excellent "bromcresol green," or tetrabrom metacresol sulphonphthalein of Cohen [7] was used, which covers the range p_H 4.0 to 5.6. For determinations above p_H 5.4, bromcresol purple was used (range p_H 5.2 to 6.8).

RESULTS

A series of 124 p_H determinations on the stools of the twenty-seven infants is given in the table, classified according to age in days. The average p_H values for each day of life are plotted in the chart.

This table and chart show that the p_H changed from an average of p_H 6.1 on the day of birth to an average of p_H 4.9 on the ninth to fifteenth



The p_H of the feces in relation to the age of the infant in days.

days, inclusive. From the sixth day, the p_H tended to maintain a constant level, averaging from p_H 4.8 to 4.9. The extreme range of the determinations made on and after the sixth day was p_H 4.3 to 5.3, with 80 per cent of the determinations falling within the range p_H 4.6 to 5.2. The stools on the first day were taken from one to twenty-four hours after birth, but no significant difference in samples from the same day was noted. The values are p_H 6.1 for the first day, p_H 6.0 for the second, p_H 5.5 for the third, p_H 5.2 for the fourth, p_H 5.0 for the fifth, and p_H 4.8 for the sixth day, respectively. The average p_H drops smoothly and gradually from the first to the sixth day.

A change occurred in the color and character of the stools, coincident with these changes in acidity. On the first and second days the specimens all had the dark brownish-green color and viscid consistency characteristic of meconium. By the third or fourth day, the color was

6. Clark, W. M.: The Determination of Hydrogen Ions, Baltimore, 1922.
7. Cohen, B.: Bromcresol Green, Proc. Soc. Exper. Biol. & Med. **20**:124, 1922-1923.

greenish-yellow, and by the fourth or fifth day, the stools were, in most cases, the golden-yellow characteristic of stools following breast milk feeding.

Six of the twenty-seven infants later received supplementary feeding with cows' milk modification containing added carbohydrate, and the effect was noted in four. The p_H changed uniformly and promptly toward greater alkalinity. Another infant, artificially fed from the first to seventh day, whose stools during this period varied from p_H 5.6 to 6.1, was put on exclusive breast feeding on the eighth day. The stool p_H on the twelfth day was 5.1.

COMMENT

The smooth, orderly progression of the hydrogen ion concentration of the stools of new-born infants shows an increase in the acidity of the

P_H Determinations of Breast-Fed Infants' Stools According to Age in Days

First Day	Second Day	Third Day	Fourth Day	Fifth Day	Sixth Day	Seventh Day	Eighth Day	Ninth Day	Tenth Day
p_H 6.3	p_H 6.6	p_H 5.2	p_H 5.1	p_H 5.1	p_H 4.4	p_H 4.4	p_H 4.9	p_H 5.0	p_H 5.0
5.8	5.6	5.5	5.6	4.7	4.8	4.3	4.6	4.6	4.7
6.1	5.6	5.7	5.4	5.5	5.0	4.7	4.3	4.3	4.8
6.1	6.4	5.5	4.7	4.7	4.8	4.8	5.2	5.0	4.9
5.8	6.0	5.0	5.3	4.5	5.2	4.4	5.2	4.5	4.6
5.7	6.0	5.5	6.5	5.0	4.5	4.7	4.9	5.1	5.1
6.3	5.8	5.2	5.2	5.4	4.4	4.8	5.0	4.5	4.8
5.8	5.8	5.6	5.3	4.8	4.8	5.1		5.0	5.4
6.3	5.7	5.7	5.4	—	5.2	5.0		—	4.6
6.2	5.9	5.9	4.9			5.3			4.7
6.1	5.7	5.6	5.5			—			4.9
6.4	6.3	—	5.0						4.6
6.0	6.1		5.1						5.2
6.2	6.1		5.1						4.7
—	6.1		—						5.0
	6.0								4.9
	5.7								4.8
	6.3								4.9
Numerical average	—								5.1
p_H 6.08	5.98	5.49	5.22	4.90	4.79	4.75	4.87	4.87	4.88

contents of the lower part of the intestinal canal, simultaneous with the exercise of the digestive function.

The main factors which influence the acidity of the stools are: 1. Bacterial flora. 2. The protein content of the diet. 3. The carbohydrate content of the diet. 4. Fat content of the diet. 5. Alkalinity of the diet. 6. Starvation.

Bacterial Flora.—The intestinal tract is sterile at birth, but directly thereafter, a bacterial flora becomes established. The predominating type or types of bacteria may vary greatly. During the first day of life, even if the meconium is not sterile, the organisms are few and recently implanted. Therefore, it seems reasonable to suppose that they do not affect the acidity of the stool.

Tisdall and Brown [5] believe that "the acidity of the stools is dependent on intestinal fermentation, and that the degree of acidity varies with the extent of the intestinal zone of fermentation, the kind of carbohydrate, and the state of health of the intestinal cells." Some authors still hold that the type of predominating organism is the determining factor of the acidity of the intestinal contents. The most modern view, advanced by Ylppö [4] and by Czerny and Keller,[8] is, on the contrary, that the acidity determines the type of intestinal flora. Adam [9] found that, following breast milk feeding, enterococci which characteristically predominate in the meconium are supplanted early in the transition from meconium to feces by organisms more resistant to acid mediums. Studying the optimal p_H for various bacteria, he found that as the acidity of the medium changes, the existing growth is superseded and a new flora predominates. From this he concluded that the meconium is less acid than stools which follow breast milk feeding. Breast milk produces a characteristic acid reaction of the stool; *B. bifidus* and the gram positive flora predominate. Cow's milk produces a neutral or alkaline reaction of the stool; *B. coli, B. lactis aerogenes* and gram negative flora predominate.[10] Ylppö [4] demonstrated that after a fast of twelve to twenty-four hours, infants on either diet passed stools of the same p_H. The acidity seems, therefore, to be not the result but the determining factor of the bacterial flora.

Protein Content of the Diet.—The proteins and amino-acids are found in the stools in such small amounts that they can be of no importance in the consideration of stool acidity. Putrefactive bacteria may become a factor early in life, resulting in the breakdown of protein with the production of ammonia. But the ammonia is excreted in the urine; the stools have been shown by Van Slyke, Courtney and Fales [11] to contain little ammonia. The stools of breast-fed babies contain more than those of babies artificially fed. In the presence of adequate carbohydrate, fermentation takes place rather than putrefaction. No studies on the feces with pure protein diets are available. Hence, it has not been demonstrated that proteins increase or diminish stool acidity.

Carbohydrate Content of the Diet.—Carbohydrates are undoubtedly subject to fermentation in the intestine by the bacteria present, with a resulting production of organic acids, part of which may escape absorption, and appear in the stools. It has not been shown, however, that

8. Czerny, A. D., and Keller, A.: Des Kindes Ernährung, Ernährungsstörungen, und Ernährungstherapie, Leipzig und Wien, 1923.

9. Adam, A.: Ueber Darmbacterien, Ztschr. f. Kinderh. **29**:59-64, 65-67, 306-320, 1921.

10. Moro, E.: Jahrb. f. Kinderh. **61**:885, 1905. Cit. by Morse, J. L., and Talbot, F. D.: Diseases of Nutrition and Infant Feeding, New York, 1920.

11. Van Slyke, D. D.; Courtney, A. M., and Fales, H. L.: Forms of Nitrogen in the Stools of Infants, Am. J. Dis. Child. **9**:533-541 (June) 1915.

the extent of the fermentative process governs the amount of organic acids present in the stool. Lactic acid milk has been shown by Tisdall and Brown to result in alkaline stools. When the carbohydrate content of milk mixtures is made to equal that of breast milk (as, for example, in the six cases in this series on supplementary feedings), the stools do not have the acid reaction of breast-fed infants, but become alkaline. Therefore, the p_H of the stools is certainly not due to the carbohydrate alone.

Fat Content of the Diet.—Fat utilization is usually nearly complete, over 90 per cent of the intake being absorbed by breast-fed infants, and nearly as much by normal, artificially fed children. However, there is a normal daily excretion of over 3.0 Gm. of total fat, which may become much greater under pathologic conditions. This fat in the stools has been analyzed by Holt, Courtney and Fales,[12] and tabulated in fractions occurring as neutral fat, free fatty acid, and combined fatty acid or soap. Even on a diet free from fat, or during a period of fasting, some fat is found in the stools, under which conditions it appears that the body fat is being drawn on. Whether the fat in the stools is in the form of fatty acids or soaps depends chiefly on the acidity of the stool, which in turn depends on the relation of the food components to each other. According to Freund,[13] in a normal infant with normal fat absorption, a high fat intake does not change the mineral composition of the stools, while in chronic malnutrition the output of salts in the feces is considerably raised by increasing the fat in the diet. Telfer [14] has shown, however, that a relatively large fat intake increases the calcium in the stool. The fat content of colostrum is approximately the same, however, as that of breast milk. Holt, Courtney and Fales [15] give a slightly lower value for colostrum (2.83 per cent) for the first twelve days of lactation, than for established breast milk (3.26 per cent). Therefore, the fat content alone, should cause no difference in the stool.

Base Content.—Regarding the composition of colostrum, nearly all investigators agree that the mineral content is about 50 per cent higher and of practically the same composition as that of breast milk during the height of lactation. Holt, Courtney and Fales [15] give the values as 0.31 per cent for colostrum and 0.21 per cent for breast milk.

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12. Holt, L. E.; Courtney, A. M., and Fales, H. L.: Fat Metabolism of Infants and Young Children, Am. J. Dis. Child. **17**:38-42, 241-250, 423-439, 1919; ibid, **18**:107-126, 157-172, 1919.

13. Freund, W.: Physiologie und Pathologie des Fettstoffwechsels im Kindesalter, Ergebn. d. inn. Med. u. Kinderh. **3**:139-185, 1909.

14. Telfer, S. V.: Studies in Calcium and Phosphorus Metabolism, Quart. J. Med. **17**:245-259, 1924.

15. Holt, L. E.; Courtney, A. M., and Fales, H. L.: A Chemical Study of Woman's Milk, Especially Its Inorganic Constitutents, Am. J. Dis. Child. **10**:229-248 (Oct.) 1915.

The calcium and magnesium in the food, unlike the sodium and potassium, are excreted chiefly by way of the feces. They are present in the stools either as insoluble phosphates or sulphates, in which case they do not affect the acidity, or else they occur in combination with fatty acids as soaps. When more than enough bases are present to neutralize the fatty acids, carbonates are formed and excreted.

As has been shown by Birk,[16] for the first few days after birth, although the daily total base intake is low, the retention is good; excretion by way of the intestine is relatively slight. With the establishment of an adequate diet, the daily intake of bases increases to the point at which a surplus exists above the amount needed and retained by the body. Then larger amounts of base are excreted in the feces. Cow's milk contains three to four times as much base as does breast milk, and the usual cow's milk modifications also contain more. (In the four cases in which the effect of supplementary feeding with modified cow's milk was noted, a shift to the alkaline side occurred.) The base content of the diet appears to be a significant factor in determining the acidity of the stools; the greater the base content, the more alkaline the stool. Thus, foodstuffs producing fatty acids tend toward the formation of acid stools; diets rich in bases tend toward the production of soap or alkaline stools. The total of these two factors determines the acidity of the stools. Thus, breast milk and cow's milk contain approximately the same amount of fat, but the ratio of fat to base would give acid stools with the former, and alkaline stools with the latter. In the first days of life, both the fat and base are low in total amount. Their ratio is less significant than after the diet becomes adequate.

Starvation.—In the new-born infants who receive only breast feeding, is the observed increase in the acidity of the stools due to the type or amount of food ingested, or to their capacity to digest it?

Griswold[17] has shown that the stomach can function at birth; that babies are born with the ability to secrete hydrochloric acid, and with a well-developed capacity for gastric digestion, greater than that of older babies. The capacity for intestinal digestion is presumably similarly developed.

The amounts of colostrum obtained by infants during the first seven days of life are given by Czerny and Keller[8] (table 95) as: first day, 20 cc.; second day, 100 cc.; third day, 200 cc.; fourth day, 300 cc.; fifth day, 350 cc.; sixth day, 400 cc.; seventh day, 450 cc.

16. Birk, W.: Beiträge zum Physiologie der neugeborenen Kindes. III. Die Bedeutung des Kolostrums, Analysen und Stoffwechselversuche, Monatschr. f. Kinderh. **9**:515-612, 1910.

17. Griswold, C., and Shohl, A. T.: Gastric Digestion in New-Born Infants, Am. J. Dis. Child. **30**:541 (Oct.) 1925.

The caloric value of breast milk is 66.0 calories per hundred cubic centimeters. Colostrum varies in composition markedly with the day of lactation. For the first three days, the caloric value per hundred cubic centimeters is high, but the amount is small. Langstein [18] found its value to be as high as 147.7 calories per hundred cubic centimeters on the first day, falling to 97.5 calories on the second, and 70.0 calories on the third day (bomb determinations).

Calculating the caloric value of the food taken as that stated, the calories per kilogram are: 10 calories for the first day; 30 calories for the second, 45 calories for the third, 65 calories for the fourth, and not until the fifth day does nutrition become adequate. The amount of food which new-born infants obtain is inadequate to meet their nutritional needs, and results in a partial starvation.

Starvation has the same characteristics, whether it be pathologic, experimental, or the physiologic starvation of the new-born. Although food intake is cut down, the body cannot and does not cease to carry on metabolic processes, but burns its own tissues. The meconium seems comparable to fasting feces, in representing excretion by the intestine during a period of fasting. Hymanson and Kahn [19] found that the mineral composition of meconium is comparable with that of adult fasting feces as determined by Müller and Zweifel. The iron and calcium content of meconium is about the same as that of fasting feces; the phosphorus content is less, the sulphur content greater. Ylppö [4] observed that in starvation, whether the previous feeding has been breast milk, with stools averaging p_H 4.7, or cow's milk modifications, with stools of p_H 7.0 to 8.0, a stool averaging p_H 6.4 results. The acidity reaches a constant and characteristic p_H, almost identical with that found in new-born infants. The meconium is closely analogous, both in chemical composition and p_H, to the stools found in starvation. Therefore, it seems highly probable that the initial p_H of meconium and its gradual orderly change to that of breast-fed infants' stools, are due primarily to the state of partial starvation present at birth.

CONCLUSIONS

As the new-born infant begins to digest food, the acidity of the stools increases smoothly and gradually during the first five or six days of life from the meconium average to the average acidity of the stools of breast-fed infants. This acidity of the stool during the first days of life has been interpreted as the result of the inadequate nutrition of the infant.

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18. Langstein, L.; Rott, S., and Edelstein, S.: Der Nährwert des Kolostrums, Ztschr. f. Kinderh. **7**:210-225, 1913.

19. Hymanson, A., and Kahn, M.: Studies of the Intestinal Contents of Newly Born Infants, Am. J. Dis. Child. **17**:112-117, (Feb.) 1919.

SUMMARY

1. The average acidity of fourteen meconium specimens obtained on the day of birth was p_H 6.1.

2. For the first six days, the stools increased in acidity about p_H 0.2 each day.

3. The acidity characteristic of stools of breast-fed infants, p_H between 4.6 and 5.2, averaging p_H 4.9, was reached by the sixth day.

METABOLISM OF SALTS IN NEPHRITIS

II. POTASSIUM, MAGNESIUM AND SULPHATES *

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POTASSIUM

Early workers in the study of blood potassium in nephritis, Blumenfeldt [1] and, shortly afterward, Smillie,[2] reported increases of this ion in the blood. The latter considered potassium retention accountable for the development of uremic symptoms. He based this assumption on the observation that in normal persons doses of potassium chloride are nontoxic, but in nephritic subjects these salts, while still readily absorbed, are poorly excreted and toxic symptoms develop. Later workers, Myers and Short,[3] Loeb, Atchley and Palmer,[4] Denis and Hobson,[5] Wilkins and Kramer,[6] all report the blood potassium in nephritis as being practically constant at the normal level. Such exceptions to normality as these reports contain are almost insignificant in degree, and might readily be attributed to extraneous factors such as secondary anemia, when the cells, which contain the greater part of the potassium, are reduced in volume. Denis [7] was unable to discover any evidence of potassium retention in animals made nephrotoxic by the administration of uranium nitrate or sodium tartarate. Further, Wilkins and Kramer were unable to produce toxic symptoms by giving potassium chloride in doses sufficiently large to raise the blood potassium to 55 mg. per hundred cubic centimeters of blood. None of these observers has excluded tissue retention of potassium as a factor in producing toxic symptoms, nor have they proved a delayed excretion of this element by the kidney.

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* Received for publication, May 4, 1926.

* From the Wards of the Hospital for Sick Children, and from the Nutritional Laboratories of the Subdepartment of Pediatrics, University of Toronto.

1. Blumenfeldt, E.: Ztschr. f. exper. Path. u. Therap. **12**:523, 1913.

2. Smillie, W. G.: Potassium Poisoning in Nephritis, Arch. Int. Med. **16**:330 (Aug.) 1915.

3. Myers, V. C., and Short, J. J.: J. Biol. Chem. **48**:83, 1921.

4. Loeb, R. F.; Atchley, D. W., and Palmer, W. W.: J. Gen. Physiol. **4**:591, 1922.

5. Denis, W., and Hobson, S.: J. Biol. Chem. **55**:183, 1923.

6. Wilkins, Lawson, and Kramer, Benjamin: Studies on the Potassium Content of Human Serum, Arch. Int. Med. **31**:916 (June) 1923.

7. Denis, W.: J. Biol. Chem. **56**:473, 1923.

We have studied the complete metabolism of potassium in thirteen cases of nephritis. The standard gravimetric methods were used up to the point at which the sodium and potassium were separated. From there on, Green's [8] cobaltinitrate method was used in determining the potassium of the food and excreta. Kramer and Tisdall's [9] method was used in making the plasma determinations. Our results are given in table 1. The normal values of the blood potassium as given by the authors of the method used is 19.5 mg. per hundred cubic centimeters of blood. The results obtained in normal subjects by Myers and Short are comparable, while those of Denis are a little higher, from 20 to 22 mg. per hundred cubic centimeters. Care was taken to ensure rapid separation of the plasma and corpuscles, as contact between them and the relatively poorly concentrated plasma may give falsely high values.

TABLE 1.—*Complete Metabolism of Potassium in Thirteen Cases*

Name	Age	Edema	Intake	Feces	Absorbed	Urine	Balance	Blood K	Type of Nephritis
A. J.	13	Neg.	2.0790	0.2987	1.7803	2.4322	—0.6519	20.0	Acute
N. W.	10	Neg.	2.4560	0.3749	2.0820	1.9612	+0.1208	19.7	Acute
W. Ca.	10	Neg.	2.1787	0.4403	1.7384	1.5560	+0.1825	20.3	Acute
G. B.	11	Neg.	0.6177	0.0539	0.5638	0.7341	—0.1703	19.8	Acute
W. Co.	11	Neg.	2.9767	0.5329	2.4238	2.0523	+0.3715	19.8	Acute
A. C.	13	Neg.	1.7717	0.5017	1.2700	2.1669	—0.8969	19.9	Acute
G. A.	8	+	2.2219	0.2837	1.9748	2.1931	—0.2549	19.5	Cardiorenal
E. D.[1]	8	+++	1.8660	.....	.....	1.9967	—0.1298	21.5	Chronic tubular
E. D.[2]	9	+	2.2400	0.2319	2.2911	1.8965	+0.3946	21.0	Chronic tubular
I. T.	6	+	4.4164	0.3299	4.0865	2.0440	+2.4250	20.0	Chronic interstitial
R. B.	4	+	2.0241	0.2325	1.7916	1.5776	+0.2140	19.5	Acute
D. H.	3	+	.....	.....	.....	1.6521	.....	20.5	Chronic
B. H.	8	0	2.3616	0.2332	2.1284	2.6703	—0.5419	20.8	Acute
A. J.	9	0	2.2140	0.2365	1.9775	2.7009	—0.7234	19.6	Acute

The blood potassium is given in milligrams per hundred cubic centimeters of serum. All other figures are in grams. The amount absorbed is obtained by deducting the amount in the feces from the total intake.

Our cases included all types of nephritis except the arteriosclerotic. Some had nitrogen retention, a few were acidotic or uremic and a number edematous, but in no instance was there any significant rise in the blood potassium. Myers and Short [3] found such slight variations as occur in their cases to be roughly proportional to the total solids and cell volume of the serums. The chart shows how very rough any such relationship proved in our cases.

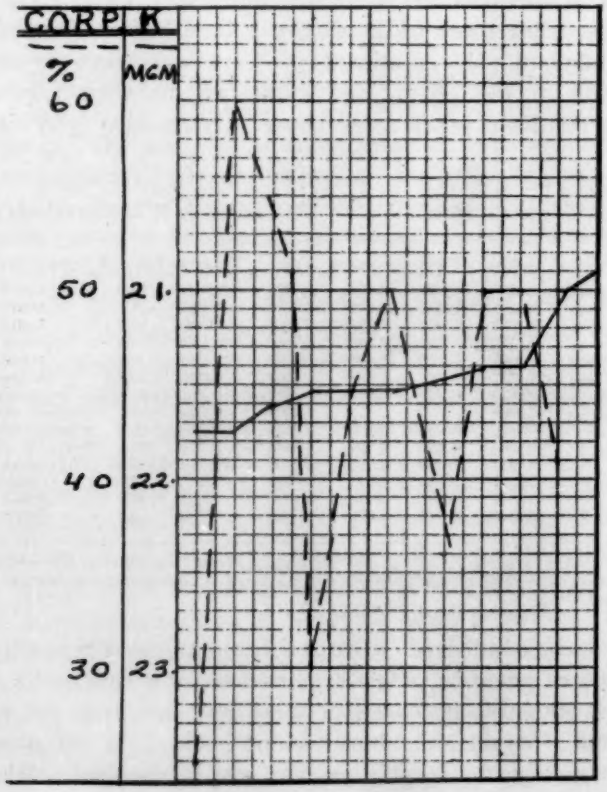
Did the balance studied furnish any evidence of a functional incapacity of the kidney to excrete these salts, or of tissue retention? For the sake of comparison, table 2 is given, containing the unpublished results obtained by one of us (A. M. C.) in a similar study of three hospital cases with no renal lesion. It is worthy of note that although

8. Green: Biochem. J. **6**:69, 1912.
9. Kramer, B., and Tisdall, F. F.: J. Biol. Chem. **46**:339, 1921.

TABLE 2.—*Potassium Balance in Normal Children in Hospital* *

Name	Age	Intake	Feces	Absorbed	Urine	Balance	Diagnosis
E. M.	..	3.9950	0.3670	3.6280	3.0820	+0.5460	Epileptic
N. T.	12	3.3329	0.4924	2.8405	2.4527	+0.3878	Epileptic
E. G.	3	1.4229	0.1679	1.2550	0.9002	+0.3548	Endocrine disturbance

* The figures in this table were obtained by one of us (A. M. C.), and have not been published as yet.



This chart shows the relationship in our cases.

all the normal children had a positive potassium balance, seven of the thirteen nephritic subjects had a negative one. This occurred in spite of the fact that the intake in the kidney cases, with one exception, was as large as that of the normal children. Further, it is of interest to note that even in those renal cases having a positive balance, its magnitude was less than that of those having no kidney lesion. This tendency to a low positive or negative balance is apparently due, in part, to defective absorption and a slightly greater loss by bowel in the nephritic

cases. There was absolutely no evidence of any impairment of renal function in excreting these salts. An appreciably larger percentage of the intake was excreted by the kidney in the nephritic than in the normal, and, further, its concentration in the urine varied from 200 to 300 mg. per hundred cubic centimeters with an average of 230 in the controls, and from 155 to 402 in the nephritics, averaging 204.

MAGNESIUM

The literature contains almost a complete dearth of material concerning the study of magnesium salts in nephritis. The few figures given by Denis are the only ones available. It might have been expected, because of their extensive clinical use in the treatment of nephritis and their sedative action, that they would have attracted more attention. In table 3 are given the results we obtained in both blood and metabolism studies of magnesium in thirteen cases of nephritis. Because of the

TABLE 3.—*Magnesium Balance in Nephritis*

Name	Age	Edema	Intake	Feces	Absorbed	Urine	Balance	Blood	Type of Nephitis
A. J.	13	Neg.	0.2173	0.1320	0.0853	0.1058	—0.0205	1.8	Acute
G. B.	11	Neg.	0.1279	0.9218	—0.7939	0.0345	—0.8284	1.78	Acute
W. Co.	10	Neg.	0.3457	0.2726	0.0731	0.0260	+0.0471	1.85	Acute
N. W.	10	Neg.	0.2726	0.2302	0.0424	0.1016	—0.0592	1.92	Acute
A. C.	13	Neg.	0.1877	0.2376	—0.0490	0.0764	—0.1263	1.79	Acute
W. Ca.	10	Neg.	0.2273	0.2095	0.0178	0.0588	—0.0410	1.90	Acute
R. B.	4	+	0.2367	0.1411	0.0956	0.0391	+0.0565	2.0	Acute
D. H.	3	+	.....	.....	.....	0.0988	.....	1.7	Chronic
G. A.	8	+	0.2686	0.1994	0.0692	0.0774	—0.0082	1.9	Cardiorenal
E. D.[1]	8	+	0.1952	.....	.....	0.2841	—0.0889	1.5	Chronic tubular
E. D.[2]	9	+	0.2619	0.1607	0.0925	0.0669	+0.0283	1.8	Chronic tubular
I. T.	6	+	0.4585	0.2388	0.2197	0.0472	+0.1725	1.9	Chronic interstitial
B. H.	8	0	0.2592	0.1706	0.0886	0.1203	—0.0317	2.0	Acute
A. J.	9	0	0.2430	0.1821	0.0609	0.0665	—0.0056	1.9	Acute

lack of such studies in normal individuals, we have given in table 4 some unpublished figures obtained by one of us (A. M. C.) in hospital patients as nearly normal as could be secured. McCrudden's methods were used in the balance experiments, and Kramer and Tisdall's [10] method in determining the magnesium of the blood. Normal values for blood magnesium obtained by Tisdall range from 2.3 to 4 mg. per hundred cubic centimeters of blood. This normal range given by Denis is somewhat lower, from 1.6 to 3.5 mg. per hundred cubic centimeters of blood.

The blood findings in our series agree with those of Denis and Hobson, who found the plasma magnesium always within normal limits. In most cases, the values obtained were the minimal regarded as normal. The question arises whether the maintenance of the magnesium at a low normal level associated with the definitely low blood calcium usually found and reported in a previous paper [11] does not reduce the sedative ions of the blood to such an extent that their ratio to the

10. Kramer, B., and Tisdall, F. F.: J. Biol. Chem. **47**:475, 1921.

11. Boyd, G. L.; Courtney, A. M., and MacLachlan, I.: The Metabolism of Salts in Nephritis, Am. J. Dis. Child. **32**:29 (July) 1926.

irritative salts, particularly sodium, is sufficiently altered to bring about an increased irritability of the neuromuscular system, and to be partially responsible for the production of uremic symptoms. Further discussion of this ratio must necessarily be dealt with in a later paper, in which the sodium ion in nephritis will be discussed. Suffice it to say here that the sum of the calcium and magnesium in our cases ranged from 8.7 to 11.7 mg. per hundred cubic centimeters of blood, as opposed to a normal value of 12 mg. per hundred cubic centimeters, and that the sodium values we obtained do not deviate far from normal. The greatest depression of the calcium-magnesium content of the serums was usually in those cases having acidotic or uremic symptoms, but in two uremic patients, one with convulsions, values of 10.58 and 10.75 mg. per hundred cubic centimeters were obtained.

Balance experiments indicate that in nephritis there is a tendency to excessive loss of magnesium salts. All types of nephritis studied, unless complicated by edema, had a negative magnesium balance.

TABLE 4.—*Unpublished Figures in Normal Subjects*

Name	Age	Intake	Feces	Absorbed	Urine	Retention
E. G.	3	0.2217	0.1351	0.0866	0.0857	+0.0009
E. M.	..	0.702	0.1900	0.5120	0.265	+0.247
N. F.	11	0.1434	0.1158	0.0276	0.1192	—0.0916

Accumulation of fluid in the body apparently results in a temporary retention, but as noted in one case (E. D.) studied with and without edema, loss of the abnormal fluid results in the establishment of a negative magnesium balance. This excessive loss was present in spite of the somewhat larger intake of the nephritic subjects than of the normal subjects.

The amounts of magnesium oxide excreted by the kidney in nephritis are comparable to that excreted by the normal children. To accomplish the excretion of these amounts, the diseased kidney apparently had to pass a larger volume of urine, as the concentration of magnesium oxide in all but two cases was much lower than in the normal subjects and the urine volume larger. Table 5 gives figures indicating the low concentrations of urine from nephritic subjects.

SULPHATES

Our attention was first attracted to the possible importance of sulphate metabolism in nephritis by the article by Denis and Hobson, referred to in the foregoing. Unfortunately, this occurred at too late a date to permit a study of sulphates in all of our cases. Denis'[12] methods were used in the blood determinations, and that of Stockholm

12. Denis, W.: J. Biol. Chem. **49**:311, 1921.

and Koch [13] in the total metabolism. Denis' figures for normal plasma sulphate are the only ones in the literature, and range from 0.5 to 0.9 mg. per hundred cubic centimeters of plasma. She found an increase in plasma sulphate in 64 per cent of the sixteen cases of nephritis studied by her, and considers the kidney's ability to excrete sulphates comparable to its power to excrete uric acid. Both are apparently difficult to excrete and therefore readily retained. Further, by means of animal experiments involving the injection of various salts, such as magnesium sulphate, sodium sulphate, magnesium chloride, sodium chloride and sodium phosphate, she demonstrated a selective retention of the sulphate ion by the kidney in animals made nephrotoxic with uranium nitrate or sodium tartarate. No constant increase of any other inorganic substance was noted.

TABLE 5.—*Concentration of Magnesium in Normal and Nephritic Urine*

Name	Amount of Urine, Cc.	Gm. of MgO in Urine	Mg. MgO per 100 Cc. Urine
Normal Subjects:			
H. B.	365	0.030	8.2
T. C.	545	0.080	15.4
G. S.	655	0.103	15.7
I. N.	630	0.129	20.4
R. H.	445	0.057	12.8
A. C.	715	0.119	16.6
Nephritic Subjects:			
B. H.	1,820	0.120	6.5
G. B.	446	0.034	7.6
A. J.	1,270	0.066	6.2
B. C.	1,158	0.026	2.2
B. Ca.	798	0.058	7.3
A. C.	1,368	0.076	5.5
Al. J.	1,371	0.105	7.6
N. W.	1,262	0.101	8.0
E. D.[1]	550	0.284	52.0
E. D.[2]	850	0.066	7.0
B. B.	710	0.039	5.5
I. T.	945	0.047	4.9
G. A.	545	0.077	14.0

In table 6 are given the results we obtained in the study of the sulphates of the blood and the total metabolism in eight cases of nephritis. Definite increases in blood sulphates were present in four cases, or 50 per cent of those studied. The significance of the increase in the plasma sulphate is difficult to determine. As a percentage increase over normal, the values found represented a tremendous rise. Even the great relative increases noted leave the sulphate ion, as an acid, a rather insignificant factor, in the acid base economy of the body. No specific toxic action has been attributed to the sulphate ion. Its increase in the blood of nephritic subjects probably indicates nothing further than an impairment of renal function which permits its accumulation in the blood.

13. Stockholm & Koch: J. Am. Chem. Soc. **45**:1953, 1923.

It is impossible to draw conclusions from our studies of sulphate metabolism in nephritis because of the entire absence of any study of sulphate metabolism in normal children. As shown in table 6, four of our cases had a negative balance; in three of these the blood sulphate was normal, and in the fourth it was only slightly increased. Positive balances were obtained in the two cases having the greatest percentage increase in their blood sulphate, and also in two in which the plasma sulphate was normal. Negative balances were found in all cases with edema, irrespective of the plasma sulphate. Urinary excretion of sulphates in cases having a positive balance, is as good or better than in those having a negative balance. This applies to both the actual amount excreted and to the concentration in a unit volume of urine. This fact might be interpreted as indicating that defective renal excretion was not responsible for the production of sulphate retention. On the other hand, the constant association of negative balances with the type of

TABLE 6.—*Results Obtained in the Study of Blood Sulphates in Eight Nephritic Subjects*

Name	Age	Edema	Intake	Feces	Absorbed	Urine	Mg. Sulphate per 100 Cc. Urine	Balance	Blood	Type of Nephritis
E. D.[2]	9	+	1.1650	0.1250	1.0398	1.0132	119	+0.0259	1.0	Chronic tubular
W. Co.	11	0	1.5877	0.3263	1.2114	0.7721	68	+0.4399	2.1	Acute glomerulo
R. B.	4	+	1.0527	0.0802	0.9725	0.6497	91	+0.3228	0.89	Acute glomerulo
N. W.	10	0	1.1260	0.1124	1.0136	1.1532	91	—0.1396	1.30	Acute glomerulo
I. T.	6	+	2.0894	0.1829	1.8565	1.1501	121	+0.7064	1.5	Chronic interstitial
G. B.	11	0	0.6072	0.5187	0.0885	0.4075	91	—0.2190	1.2	Acute glomerulo
W. H.	8	0	1.2048	0.1402	1.0646	1.2108	69	—0.1462	0.9	Acute glomerulo
A. J.	9	0	1.1296	0.1496	0.9799	1.2427	90	—0.2628	1.1	Acute glomerulo

nephritis with predominating tubular lesions and little or no nitrogen retention, which Denis found always with sulphate retention, would indicate some responsibility on the part of the kidney in determining the presence or absence of sulphate retention.

SUMMARY

1. The plasma potassium in nephritis is maintained at a constant normal level, independent of the type of nephritis or the presence or absence of toxic symptoms.

2. There is no evidence of tissue retention of potassium salts in nephritis.

3. The kidney maintains its ability to excrete potassium salts in a normal manner.

4. The magnesium of the blood plasma is at a low normal level in all types of nephritis.

5. In nephritis, there is a tendency to excessive loss of magnesium salts from the body and the production of a negative balance. The presence of edema modifies this trend temporarily.

6. The concentration of magnesium oxide in nephritic urine is usually much lower than in normal persons.

7. Plasma sulphates were increased in 50 per cent of the cases of nephritis studied.

8. Evidences of sulphate retention furnished by metabolism studies are not always in agreement with those given by blood studies.

9. There is a negative sulphate balance in nephritic edema.

10. Sulphate retention in nephritis does not appear to be due to defective urinary excretion.

COAGULATION TIME AND BLEEDING TIME IN THE NEW-BORN

EFFECT OF PROPHYLACTIC INJECTIONS OF BLOOD *

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Hemorrhage is considered the most frequent cause of death during the first week of life. In 65 per cent of all infants dying within five months, Schwartz [1] found gross signs of trauma sustained in the brain at birth, that is, hemorrhage or softening that could be discerned with the naked eye. In 50 per cent of mature infants and in 40 per cent of premature infants, Cruickshank [2] found gross signs of hemorrhage in the brain. He concludes from his figures that many new-born infants with quite extensive hemorrhage survive. Ylppö,[3] in examining the bodies of premature infants, concluded that the smaller the infant the higher was the percentage of hemorrhage. In infants weighing less than 1,000 Gm., the incidence of hemorrhage was 90 per cent, and in those weighing between 2,000 and 3,000 Gm. it was only 28 per cent. He followed 322 prematurely born children up to the age of 8 years and found that ten had spastic paralysis and that twenty-four were imbeciles.[4] He thinks there is a definite relationship between these conditions and intracranial hemorrhage. Warwick,[5] in one series of 200 new-born infants and in another of thirty-six, at necropsy found cerebral hemorrhage in 43 and 50 per cent, respectively. In 20 per cent, multiple hemorrhages were demonstrable. She believes the latter is a definite sign of hemorrhagic disease.

Rodda [6] states that the most frequent cause of hemorrhage in the new-born is trauma plus hemorrhagic disease. The subcutaneous administration of whole blood to new-born infants with prolonged coagulation or bleeding time influenced the coagulation and the bleeding time

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* Received for publication, May 4, 1926.

* From the Section on Pediatrics, Mayo Clinic.

1. Schwartz, P.: Die traumatische Geburtsschädigung des Gehirns, München. med. Wchnschr. **69**:1110-1112 (July 28) 1922.

2. Cruickshank, J. N.: The Haemorrhages of the New-Born, Lancet **1**:836-839 (April 28) 1923.

3. Ylppö, Arvo: Pathologisch-anatomische Studien bei Frühgeborenen, Ztschr. f. Kinderh. **20**:212-431, 1919.

4. Ylppö, Arvo: Zur Physiologie, Klinik und zum Schicks al der Frühgeborenen, Ztschr. f. Kinderh. **24**:1-110, 1919.

5. Warwick, Margaret: Cerebral Hemorrhages of the New-born, Am. J. M. Sc. **158**:95-105 (July) 1919; Necropsy Findings in New-Born Infants, Am. J. Dis. Child. **21**:488-499 (May) 1921.

6. Rodda, F. C.: The Coagulation Time of Blood in the New-Born, with Special Reference to Cerebral Hemorrhage, J. A. M. A. **75**:452-457 (Aug. 14) 1920.

favorably. Since Rodda's report, numerous observers have reported good results from the injection of whole blood. Warwick [7] reported thirteen cases in which the coagulation time or bleeding time, or both, were abnormally long. Treatment was instituted before symptoms of hemorrhage developed, and in eleven cases the coagulation time and the bleeding time became normal. In one, typical signs of cerebral hemorrhage appeared, but the infant recovered; another died and necropsy findings were typical of congenital syphilis. In two cases in which the desired results could not be obtained by the injection of blood, the Wassermann reaction was positive. Rosamond [8] found that seventeen new-born infants who suffered from convulsions, fourteen of whom

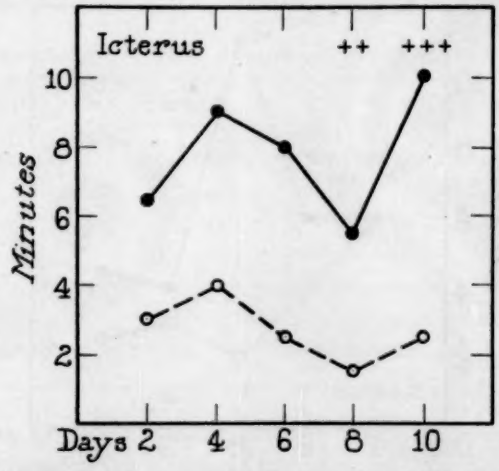

Chart 1.—In one case there was icterus from the eighth to the tenth day with slight prolongation of the coagulation time. No blood was given. In this and in the following charts, the unbroken line indicates coagulation time; broken line, bleeding time.

had a prolonged coagulation or bleeding time, responded to this form of treatment. Brady,[9] after treating twenty-two new-born infants suffering from intracranial hemorrhage, advised that blood should always be given intramuscularly. Besides the administration of blood, lumbar or cisternal puncture was done in his cases. Losee [10] reports good results in all but one of sixteen cases of hemorrhage in new-born

7. Warwick, Margaret: The Value of the Routine Determination of Bleeding and Coagulation Times Upon New-Born Infants, Minnesota Med. **5**:713-719 (Dec.) 1922.

8. Rosamond, E.: Intracranial Hemorrhage in New-Born: Case Report, South. M. J. **15**:618-619 (Aug.) 1922.

9. Brady, J. M.: Cisterna Puncture in Intracranial Hemorrhage of the New-Born, Am. J. Dis. Child. **28**:122 (July) 1924.

10. Losee, J. R.: Hemorrhages in New-Born, Bull. Lying-In Hosp. **12**:100-106 (July) 1922.

infants, who were treated by blood transfusion. Eight had previously been treated with normal human serum without result. Capon [11] treated six infants with blood and horse serum: five recovered and one died.

Within a relatively short period, several new-born infants seen in the Section on Obstetrics of the Mayo Clinic presented signs of hemorrhage from the bowels or navel. The hemorrhage ceased promptly in nearly every case after the subcutaneous administration of from 10 to 20 cc. of whole blood. Two other infants, one of whom was premature, died within a week of birth without any sign of hemorrhage, but at necropsy evidence of rather extensive hemorrhage was found in the cranium. For some time afterward, every new-born

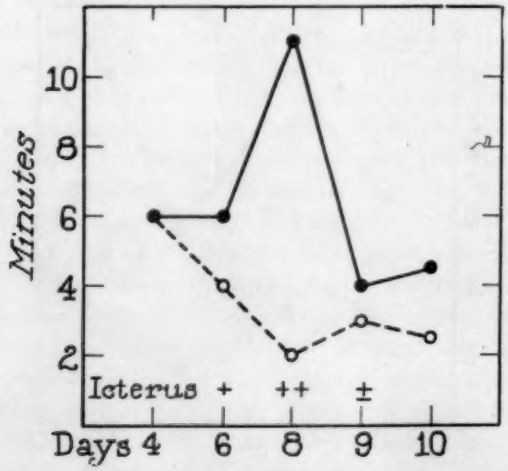

Chart 2.—In a second case there was marked icterus on the eighth day, with slight prolongation of the coagulation time. No blood was given.

infant whose parents did not object received an injection of from 10 to 20 cc. of whole blood as a prophylactic measure.

It may be assumed, therefore, that intracranial injury at birth is of rather frequent occurrence. Injection of blood may aid in diminishing the resulting danger from it and prevent further complications when the coagulation and the bleeding times are prolonged.

In order to determine whether such injections did have an influence on the coagulation time and the bleeding time of new-born infants, studies were made on 125 infants, chosen at random. For the determination of the coagulation time the method employed by Rodda [12] was

11. Capon, N. B.: Haemorrhagic Disease of the New-Born, with Reports of Six Cases, Lancet **1**:1203-1206 (June 14) 1924.

12. Rodda, F. C.: Studies with a New Method for Determining the Coagulation Time of the Blood in the New-Born, Am. J. Dis. Child. **19**:269-276 (April) 1920.

used, and for the determination of the bleeding time, the method used by Duke.[12]

The coagulation time and the bleeding time were determined a total of 377 times in these infants. Sixty-eight infants who did not receive any blood served as controls: forty received 10 cc. each, and seventeen, 20 cc. of fresh whole blood subcutaneously. The blood was injected between the scapulas, and the slight swelling resulting was gently massaged. After twenty-four hours no sign of the injection remained, except in a few cases in which a slight discoloration of the skin persisted for several days. The coagulation and the bleeding times were determined before the injection of blood and every second day as long as the infant remained in the hospital, usually from eight to ten days.

TABLE 1.—*Prolonged Coagulation and Bleeding Times*

Coagulation Time, Minutes	Amount of Blood Injected			Bleeding Time, Minutes	Amount of Blood Injected		
	0 Cc.	10 Cc Cases	20 Cc.		0 Cc.	10 Cc. Cases	20 Cc.
11	5	2	1	6	1	3	0
12	3	0	0	7	1	1	0
13	0	1	1	8 to 9	6	2	0
14	0	0	0	10 to 15	4	2	0
15 to 20	2	1	1	More than 15	3	2	0
Total	10	4	3		15	10	0
Normal coagulation time	58	36	14	Normal bleeding time	53	30	17

According to Rodda, coagulation time varies from six to ten minutes, the average being seven minutes; the bleeding time varies from two to five minutes, the average being three and one-half minutes (table 1). To eliminate personal variation, I made all the determinations myself. In seventeen instances, after injection of blood the coagulation time exceeded ten minutes, the limit which Rodda considered normal. It is agreed that this limit is purely arbitrary. The number of determinations is too small to warrant definite conclusions, but the injection of blood did not seem to influence the coagulation time. Bleeding lasted longer than five minutes, the arbitrary limit for normal, in twenty-five instances. The striking feature is that none of the new-born had a bleeding time of more than five minutes after treatment with 20 cc. of blood. The longest bleeding time before treatment was thirty-six minutes. Table 2 gives the instances of prolonged coagulation time and bleeding time according to the days on which they were observed.

13. Duke, W. W.: The Relation of Blood Platelets to Hemorrhagic Disease. Description of a Method for Determining the Bleeding Time and Coagulation Time, and Report of Three Cases of Hemorrhagic Disease Relieved by Transfusion, J. A. M. A. **55**:1185-1192 (Oct. 1) 1910.

These figures agree with those of Lucas and Rodda, who found that the incidence of prolongation is more frequent in the first five days of life.

Twenty-one new-born infants who did not receive blood and twelve who received an injection of 10 cc. had a prolonged bleeding time or coagulation time, or both. Of seventeen new-born infants, after the administration of 20 cc. the coagulation time was prolonged in three, but in none was the bleeding time prolonged (table 3). The average bleeding time for the group in which 20 cc. of blood had been given was two and one-half minutes.

TABLE 2.—*Instances of Tests for Prolonged Coagulation and Bleeding Times*

Day of Test	Cases with Prolonged Coagulation Time: Amount of Blood Injected			Cases with Prolonged Bleeding Time: Amount of Blood Injected		
	0 Cc	10 Cc	20 Cc.	0 Cc.	10 Cc.	20 Cc.
1	2	0	0	1	0	0
2	1	2	1	1	1	0
3	1	0	2	2	1	0
4	2	0	0	5	1	0
5	1	2	1	2	2	0
6	0	1	0	1	2	0
7	1	0	0	3	2	0
8	1	0	0	1	1	0
9	1	0	0	1	0	0

TABLE 3.—*Summary of Cases*

Amount of Blood Injected, Cc.	Cases	Cases with		
		Prolonged Coagulation Time	Prolonged Bleeding Time	Prolonged Coagulation and Bleeding Times
0	68	6	11	4
10	40	2	8	2
20	17	3	0	0
Total	125	11	19	6

The figures are too few to make a percentage analysis. The incidence of the prolongation of the coagulation time and of the bleeding time in the groups in which no blood was given, and in that in which 10 cc. was injected, is about the same. It seems safe, therefore, to conclude that 10 cc. of blood injected subcutaneously in new-born infants does not exercise any definite effect on the coagulation or bleeding time. The injection of 20 cc. of blood seems to have a definite effect on the bleeding time but not on the coagulation time.

Since the coagulation time is often prolonged in cases of severe icterus of long duration, I studied icterus of the new-born while making determinations of the coagulation and the bleeding times.

Ylppö,[14] in 1913, observed that in icterus neonatorum the intensity of the jaundice is definitely related to the amount of bile pigment in the blood. New-born infants have a larger amount of bile pigment in the blood than healthy adults. Usually, bile pigment increases from the eighth to the tenth day; then decreases gradually to normal. Eighty-two per cent of the new-born infants seen by Ylppö [14] had icterus of the skin. Lucas [15] and his co-workers found an increase in bilirubin in seventy-two of ninety new-born infants.

The observations on the coagulation time and bleeding time in icterus neonatorum are contradictory. Flusser,[16] who employed Wright's

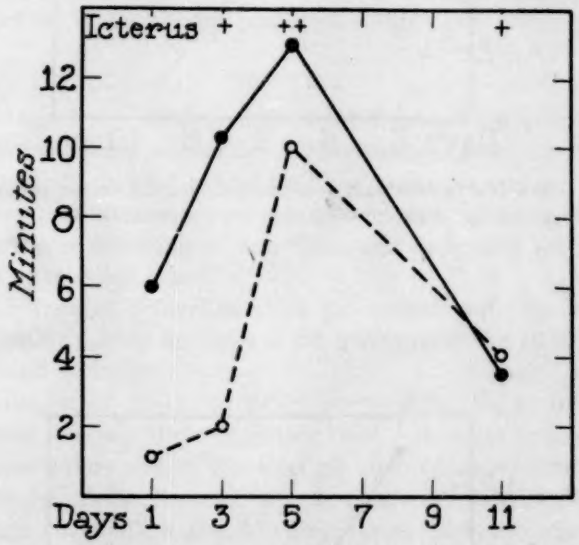

Chart 3.—In a third case there was marked icterus, with prolongation of both coagulation and bleeding times four days after 10 cc. of blood had been given.

method of determining the coagulation time of the new-born with icterus, noted that prolongation did not parallel the intensity of the jaundice. Greuter,[17] employing Burker's method, found prolongation of the coagulation time in 75 per cent of jaundiced new-born infants

14. Ylppö, Arvo: Icterus neonatorum und Gallenfarbstoffsekretion beim Foetus und Neugeborenen, Ztschr. f. Kinderh. **9**:208-318, 1913.

15. Lucas, W. P.; Dearing, B. F.; Hoobler, H. R.; Cox, Anita; Jones, Martha R., and Smyth, F. S.: Blood Studies in the New-Born, Am. J. Dis. Child. **22**: 525-559 (Dec.) 1921.

16. Flusser, E., quoted by Greuter: Untersuchungen über die Gerinnbarkeit des Blutes in den ersten Lebenswochen, Monatschr. f. Kinderh. Orig. **12**:705-713, 1914.

17. Greuter, Werner: Die Blutgerinnungszeit bei Icterus neonatorum, Ztschr. f. Kinderh. **35**:210-226 (June) 1923.

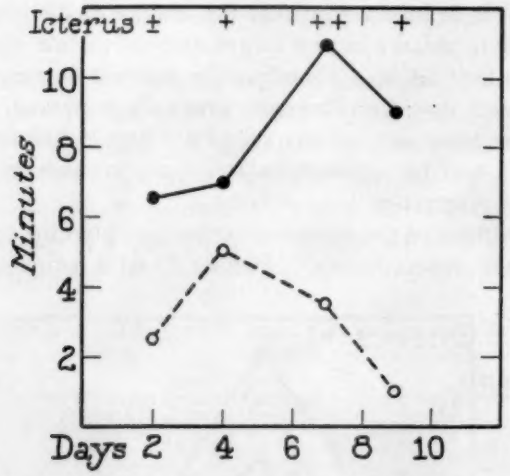

Chart 4.—In a fourth case there was marked jaundice on the seventh day after birth, accompanied by slight prolongation of the coagulation time. No blood was given.

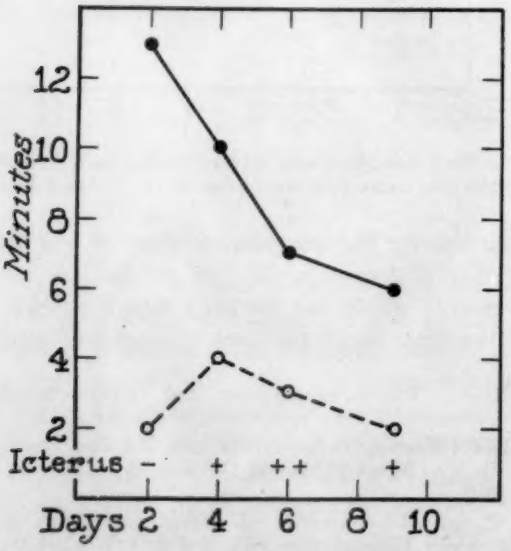

Chart 5.—In a fifth case, 20 cc. of blood was given on the day of birth. Twenty-four hours later the coagulation time was found to be prolonged. It gradually became normal, although the jaundice increased.

during the first ten days of life. Rodda observed normal coagulation and bleeding times in infants with icterus neonatorum.

In this series, five cases were observed in which there seems to be a definite relationship between the intensity of the icterus and the length of the coagulation time and bleeding time. The degree of icterus was judged by the discoloration of the skin and scleras (charts 1 to 5). The average coagulation and bleeding times in these infants were the same as in new-born infants without jaundice. In one case of jaundice, the coagulation time was twelve minutes and the calcium time six minutes. This suggests that the administration of calcium may be of benefit in cases of jaundice in infants with prolonged coagulation time, as advocated by Walters [18] for jaundiced adults.

SUMMARY

In 125 new-born infants, the coagulation and the bleeding times were determined every second day. Forty infants received 10 cc. each, and seventeen, 20 cc. of fresh whole blood subcutaneously. The sixty-eight infants who received no blood served as controls. Neither the giving nor the withholding of treatment was dependent on the coagulation time or bleeding time.

The incidence of prolongation of the coagulation time and of the bleeding time was about the same in the group receiving 10 cc. as in that which received no blood.

The injection of 20 cc. of blood seems definitely to influence the bleeding time, but not the coagulation time. A slight prolongation of the coagulation time and of the bleeding time appeared simultaneously with the height of the jaundice in a few cases of icterus neonatorum. The average coagulation and bleeding times, however, corresponded closely with those of new-born infants without icterus.

The results in this small series indicate that the administration of 10 cc. of blood is of little value. When blood is administered as a prophylactic measure against bleeding, at least 20 cc. should be given.

18. Walters, Waltman: Preoperative Preparation of Patients with Obstructive Jaundice, Surg., Gynec. & Obst. **33**:651-656 (Dec.) 1921.

CEREBROSPINAL FLUID IN THE NEW-BORN *

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During the last few years, there appeared a number of articles on lumbar puncture in the new-born, with special reference to cerebral hemorrhage. With one exception,[1] the authors who have written on the subject believe that lumbar puncture is indicated in suspected cases of cerebral hemorrhage. Lippman [2] expresses his opinion that "the finding of blood in spinal fluid is not sufficient to make a diagnosis of cerebral hemorrhage, as it may be due to the puncture of a vessel." All other authors, however, believe that blood-stained cerebral fluid obtained by lumbar puncture may be taken as an indication of the presence of cerebral hemorrhage. This opinion has especially been held by Green,[3] Brady,[4] Roberts,[5] Sharpe and Maclaire.[6] The last two authors consider lumbar puncture as an accurate method of diagnosis of cerebral hemorrhage, and advise the repetition of lumbar puncture as a therapeutic measure until the fluid becomes clear. The opinion has also been expressed in the literature [5] that it is easy to differentiate bloody cerebrospinal fluid due to puncture trauma from that due to cerebral hemorrhage.

During the last few months, in order to determine the asymptomatic occurrence of cerebral hemorrhage at the earliest possible moment, we removed cerebrospinal fluid from a series of new-born infants in the hope of diagnosing. And, if found practical, of treating patients suspected to be suffering from cerebral hemorrhage, as suggested by Sharpe and Maclaire.

Our work was done at the obstetric ward of the Cook County Hospital. With very few exceptions, the fluid was removed within twenty-

* Received for publication, May 1, 1926.

1. Grulee, C. G.: Treatment of Intracranial Hemorrhage in the New-Born, J. A. M. A. **85**:336 (Aug. 1) 1925.

2. Lippman, M. J.: Meningeal Hemorrhage in the New-Born, New York M. J. **103**:263 (Feb. 5) 1916.

3. Green, R. M.: Intracranial Hemorrhage in the New-Born, Boston M. & S. J. **170**:682 (April 30) 1914.

4. Brady, J. M.: Lumbar Puncture in Meningeal Hemorrhage of the New-Born, J. A. M. A. **71**:347 (Aug. 3) 1918.

5. Roberts, M. Hines: The Spinal Fluid in the New-Born with Especial Reference to Intracranial Hemorrhage, J. A. M. A. **85**:500 (Aug. 15) 1925.

6. Sharpe, William, and Maclaire, S.: Intracranial Hemorrhage in the New-Born, J. A. M. A. **88**:332 (Jan. 30) 1926; ibid., Am. J. Obst. & Gynec. **9**:452 (April) 1925, and numerous other articles.

four hours after birth. As a routine, a Wassermann test of the blood was made on all expectant mothers. If for some reason or other this had been omitted during pregnancy, the Wassermann test was made on placental blood. The cerebrospinal fluid was always examined shortly after withdrawal from the body, to avoid errors due to changes in the fluid on standing.

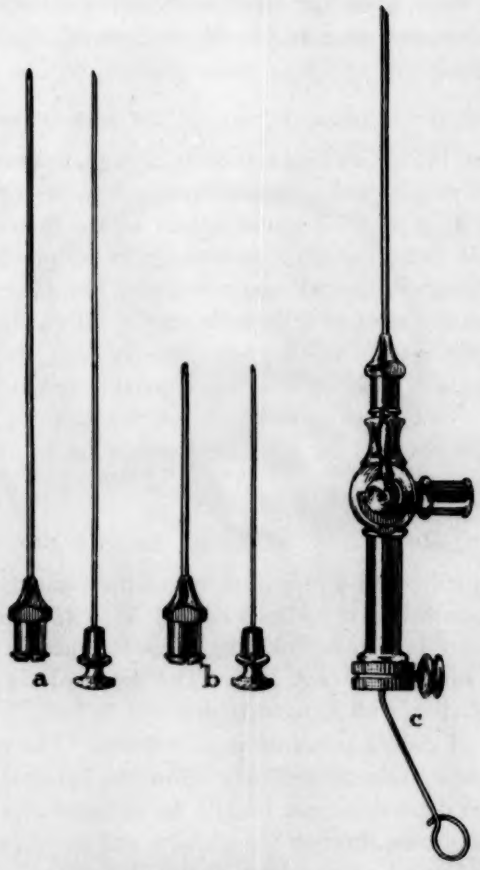

Fig. 1.—Needles for spinal and cistern puncture. *a*, for adults; *b*, for new-born infants; *c*, special needle for attachment to manometer.

METHOD OF OBTAINING FLUID

As far as we could ascertain, the examination of cerebrospinal fluid in the new-born, reported in the literature, was made on fluid obtained by the lumbar route. The difficulty of obtaining sufficient fluid, and above all, of obtaining clear fluid by means of lumbar puncture, is known to every physician who has attempted to do this work on the new-born. We, therefore, resorted to cistern puncture in some cases.

We studied 100 new-born infants for evidence of cerebral hemorrhage. In twenty-four, we obtained the fluid by means of lumbar puncture; in sixty-four, by cistern puncture, and in twelve by both routes. The number of punctures performed on the 100 subjects totaled 112, of which thirty-six were lumbar and seventy-six cistern.

In addition to the 100 patients from whom we were successful in obtaining fluid, there were five from whom we were unable to obtain any. Spinal punctures were employed in three of these, and cistern punctures in two.

TECHNIC OF LUMBAR PUNCTURE IN THE NEW-BORN

Short needles, 1½ inches long and 20 to 22 gage, were used (fig. 1-b). We found that it usually took from a few seconds to two or three minutes before the first drop of fluid would appear at the base of the needle. There was ample time to attach a manometer to the needle without loss of fluid, even though a stopcock was not used. For safety's sake, however, we occasionally used an adjustable needle with a stopcock devised by one of us (fig. 1-c). We learned that dry taps are less frequent when the puncture is done in the first lumbar interspace than in the second or third. The depth of the needle varied from ½ to 1¼ inches, depending on the size and on the subcutaneous fat of the baby. The average depth was ⅔ inch.

TECHNIC OF CISTERN PUNCTURE IN THE NEW-BORN

The needle used for cistern puncture was the same as that used for spinal puncture, namely, 1½ inches long and 20 to 22 gage. Because of the higher pressure in cistern fluid, the adjustable needle with the stopcock was more often used (fig. 1-c). The depth of the needle varied from ¾ to 1½ inches, with an average depth of ⅘ inch.

The technic of cistern puncture is as follows: The needle is introduced into the depression immediately below the external occipital protuberance. This depression can usually be palpated through the skin. Generally, a line drawn through the glabella and the upper edge of the external auditory meati passes through this depression. The needle is introduced forward, and is then directed slightly downward to avoid the resistance of the lower occipital crest (fig. 2). After the downward curve is made, and the crest avoided, the needle is again directed forward and slightly upward until the resistance caused by the atlanto-occipital ligament and dura is broken through. The stylet is then removed and the fluid is permitted to flow out.

The danger of striking the medulla during a cistern puncture should be kept in mind. We have witnessed one cistern puncture which was followed by respiratory failure, seemingly due to damage to the respira-

tory center. This can usually be avoided by taking care not to introduce the needle too far, and by removing the stylet as soon as the resistance of the atlanto-occipital ligament and dura is overcome.

In one of our cases in which a cistern puncture was performed, a circumscribed edema developed at the site of the puncture. In another case, cistern puncture was followed by bleeding from the wound. However, both the edema and the hemorrhage subsided.

In comparing the two methods of puncture, lumbar and cistern, we find that fluid can be obtained more easily by the cistern than by the

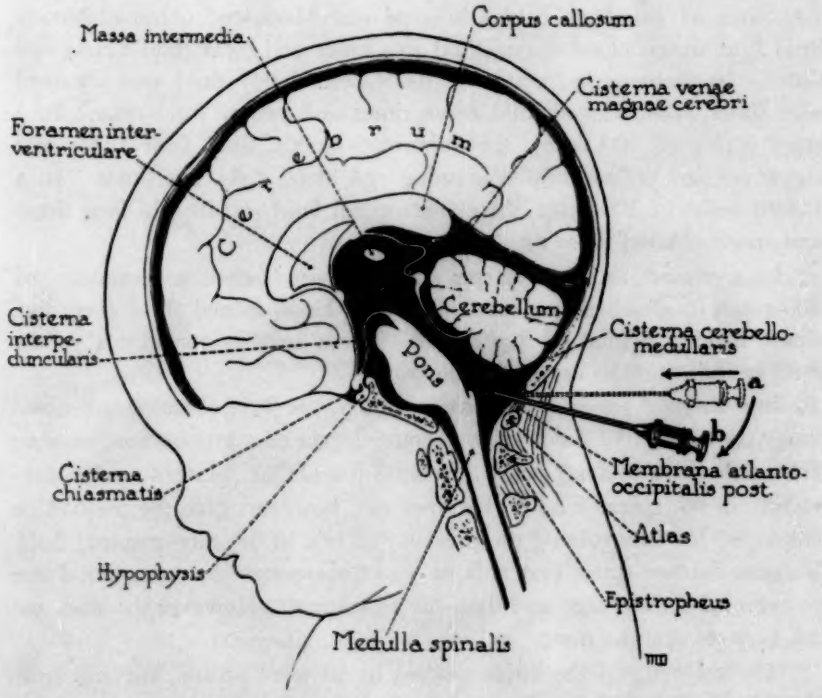

Fig. 2.—Median section of brain and coverings, showing needle in cisterna magna.

lumbar route. Out of thirty-nine attempts to withdraw fluid by the lumbar route, we had three dry taps, whereas out of seventy-eight attempts at cistern puncture, we had only two dry taps.

Traumatic blood was more frequently obtained by lumbar than by cistern puncture. There is an additional disadvantage of the lumbar puncture, in that it necessitates the removal of the abdominal binder, thus exposing the umbilical cord dressing and increasing the chances for infection.

AMOUNT OF FLUID OBTAINED

The amount of fluid obtained varied with the site of puncture. The amount obtained by spinal puncture ranged from a few drops to 5 cc., with an average of 3 cc. The amount obtained by cistern puncture varied from 1.5 to 10 cc., with an average of 6 cc.

COLOR

Of all the properties of cerebrospinal fluid in the new-born, its color has been studied the most. The reports in the literature on the color of cerebrospinal fluid in the new-born do not agree. In one series of 100 cases of new-born babies, Sharpe and Maclaire [6] obtained bloody fluid four times, blood tinged fluid five times and clear fluid ninety-one times. In their second series of 100 cases, bloody fluid was obtained nine times, blood tinged fluid three times and yellow fluid once. In a third series of 100 cases, they obtained bloody fluid four times and straw colored yellow fluid containing red blood cells, six times. In a fourth series of 100 cases, the cerebrospinal fluid was bloody four times and straw colored three times.

In a recent article, Sharpe and Maclaire [6] gave a summary of 500 cases in which they found bloody or blood tinged fluid forty-five times, making a total of 9 per cent. These authors consider a yellow fluid an indication of cerebral hemorrhage.

In Roberts' [5] series of 423 cases, none of the fluid obtained was absolutely colorless. All fluids showed some degree of pigmentation, varying from pale straw to deep yellow. Roberts found that "bilirubin exists constantly in the spinal fluid." He does not, however, give the method he employed for determining the presence of bile in the cerebrospinal fluid. Roberts further states that it is easy to differentiate between blood due to cerebral hemorrhage and that due to trauma. However, he does not tell how this can be done.

The majority of the fluids studied by us were yellow, varying from light to golden yellow. Twelve fluids were entirely colorless, twenty-four were blood tinged and four were distinctly bloody. The remainder of the 100 fluids were yellow in color, varying from light to golden yellow. As will be seen later, we cannot explain the yellow color on the basis of bile pigment.

We found it hard to differentiate blood in cerebrospinal fluid due to trauma during puncture from that due to cerebral hemorrhage. We, therefore, believe that the mere presence of fresh blood in the fluid is not a positive sign of cerebral hemorrhage, as it may be due to trauma during the puncture.

PRESSURE

We determined the pressure by means of a mercury manometer. The pressure varied according to the site of puncture. In fluid obtained by lumbar puncture, the pressure varied from 1 mm. to 6 mm. of mercury, with an average of 4.5 mm. There were two exceptions to the foregoing: one case which had a pressure of 20 mm. and the other of 16 mm.

Comparison of Spinal and Cistern Fluid in Same Patient

Case	Age, Hours	Race	Route of Puncture	Depth of Needle, Inches	Amount of Fluid in Cc.	Pressure: Manometer Reading in Mm. of Mercury	Pressure: Rate of Flow	Color
1	15½	Colored	Spinal.....	⅝	Few drops	4	.....	Clear yellow
			Cistern.....	⅝	5	8	.....	Clear yellow
2	16	White	Spinal.....	¾	1	4	.....	Clear yellow
			Cistern.....	1¼	3	18	.....	Turbid yellow
3	6½	White	Spinal.....	⅝	0.5	6	.....	Clear yellow
			Cistern.....	⅞	6	20 (baby quiet) 26 (baby crying)	.....	Clear yellow
4	23	White	Spinal.....	¾	...	6		
			Cistern.....	1¼	8	18 quiet 26 crying	Spurt	Colorless
5	12	White	Spinal.....	½	1	1	Drop every 5 seconds	Faint yellow
			Cistern.....	1¼	4	10	Spurt	Blood tinged
6	19	White	Spinal.....	⅝	Few drops	2	Drop every 20 seconds	Clear yellow
			Cistern.....	1¼	3	14	Drop every 3 seconds	Blood tinged
7	9	Colored	Spinal.....	½	1	2	.....	Blood tinged
			Cistern.....	1	3	8		
8	47	White	Spinal.....	⅝	4	4	.....	Blood tinged
			Cistern.....	1½	6	Varied between 20 and 30	Very rapid	Blood tinged
9	3	Colored	Spinal.....	½	1	2	Very slow	
			Cistern.....	1⅝	8	40	Very rapid	Blood tinged
10	26	Colored	Spinal.....	½	2	2	Few drops	Clear yellow
			Cistern.....	1	3	8	18 quiet 30 crying	Blood tinged
11	28	White	Spinal.....	¾	No fluid obtained			
			Cistern.....	1⅛	7	15	Spurted	Clear yellow
12	20	Colored	Spinal.....	½	½	3	Drop every 10 seconds	Clear yellow
			Cistern.....	1	5	36	Spurted several feet	Blood tinged

In cistern fluid, the pressure ranged from 4 to 40, with an average of 25 mm. of mercury (see the table). Sharpe and Maclaire consider a spinal pressure reading above 5 mm. of mercury as an indication of cerebral hemorrhage. Our findings seem to indicate that spinal pressure readings above 6 mm. of mercury speak for the presence of some pathologic change, possibly cerebral hemorrhage. However, we cannot consider increased pressure as a positive indication of cerebral hemorrhage, as any irritation of the meninges will increase the cerebrospinal fluid pressure.

It should also be kept in mind that the position of the needle, the type of needle and manometer used and the condition of the patient, whether quiet or crying, will change the pressure readings.

RATE OF FLOW

The rate of flow is influenced, even more than the pressure readings, by several factors, especially by the position of the needle. In most instances, the rate of flow resulting from spinal puncture varied in our series from 1 drop per second to 1 drop every thirty-five seconds; after cistern punctures, in most instances, the fluid at first spurted from the needle, flowing in a steady stream for a few seconds, and later slowing down to the rate of 1 drop per second.

CELLS

We studied the total number of red and white cells, paying particular attention to the presence of crenated cells.

The method we employed was as follows: The total number of cells in undiluted cerebrospinal fluid was first counted under low power magnification, and then recounted under high power magnification, particular attention being paid to crenated cells and to the form of white cells. As a check on the white count, glacial acetic acid was then drawn up to point 1 in the white pipet, and cerebrospinal fluid to point 11, and the white cells in all the 9 squares counted. By multiplying the result by the factor 11/9, the number of white cells per cubic millimeter was obtained. As our work advanced, we found that we could obtain just as good results by doing away with the glacial acetic acid dilution for the white count, simply counting all the cells under low power magnification and then the red, crenated and white cells under high power magnification. Four square millimeters were counted, and the result was multiplied by 2½ to allow for the depth of the chamber.

We found large numbers of red blood cells not only in the bloody or blood-tinged fluid, but also in the clear yellow fluid. We believe that the presence of most of the cells could be explained on the basis of trauma by the needle, although it is possible that in some cases the cells might have been due to cerebral hemorrhage.

We found no relation between the number of cells and the globulin tests. In some cases in which there were many cells, the globulin tests were negative. In other cases, in which there were only 6 cells, the globulin tests were positive.

Crenated cells were present in over half of the fluids examined. Their presence had no relation to the globulin increase, many crenated cells being found in fluids with negative globulin. Crenated cells were most commonly found in fluids containing large numbers of cells. This,

however, was not always the case. One fluid containing 15 cells had 8 crenated cells; another fluid containing 180 cells had 95 crenated cells; two fluids, one with 750 and the other with 14,050 cells, contained no crenated cells. Of greater importance seems to be the relation of crenated cells to the amount of fluid obtained. The more fluid obtained, the more crenated cells were found in it.

CHEMICAL TESTS FOR BLOOD

The benzidine test was found definitely positive in twelve blood-tinged fluids, and faintly positive in two blood-tinged fluids. There was also a suggestion of positive benzidine in three clear yellow fluids. The remainder of the fluids gave negative benzidine tests. The negative benzidine test would tend to show that the yellow color of the fluid is not due to hemoglobin, although it is possible that some compound of blood which does not give the benzidine reaction is responsible for the yellow color.[7] There is a possibility that the yellow color may be due to uric

7. Since the completion of this paper we encountered two cases in which clear yellow cerebrospinal fluid was obtained during life, and in which necropsy revealed cerebral hemorrhage. In one of the fluids the benzidine test was positive and in the other it was negative. The second case seems to corroborate the hypothesis stated above that the yellow color of the fluid may be due to some blood compound which no longer gives a benzidine test.

The first patient (Baby H.), 3 days old, admitted to the premature station of the Sarah Morris Hospital, May 13, 1926, gave a history of premature birth (six weeks before term), forceps delivery, attacks of cyanosis and failure to gain in weight. The patient weighed 2,020 Gm. on admission. At 21 days of age, the child developed jaundice and began to lose weight rapidly.

A spinal puncture was made on the twenty-first day of life. Eight cubic centimeters of clear yellow fluid was obtained under increased pressure. Both the globulin and the benzidine tests were positive. The fluid also contained many crenated cells.

The patient developed a terminal pneumonia and died at 26 days of age.

The postmortem examination made by Dr. Enzer showed an adherent, dark green, subarachnoid clot over the inferior and superior surfaces of the cerebellum.

The second patient (Baby K.) was admitted on May 31, 1926, to the premature station of the Sarah Morris Hospital, two hours after birth. There was a history of premature birth (calculated fetal age 29½ weeks) and a marked cyanotic spell immediately after birth. Twelve days after admission the child was slightly jaundiced and took its feedings poorly. A diagnosis of atelectasis was made, in addition to the primary diagnosis of cerebral hemorrhage. The fontanels became depressed.

Fourteen days after admission spinal puncture was performed and 6 cc. of clear yellow fluid was obtained. The fluid contained 70 cells per cubic millimeter, most of them being crenated. The benzidine test was negative. The globulin, Wassermann and Lange tests also were negative. The patient died at the age of 15 days.

On postmortem examination, made by Dr. Enzer, a dark green subarachnoid clot was found over the curvature of the cerebellum extending over the inferior and slightly over the superior surfaces. The base of the brain was free from adhesions, thickening or any other abnormalities.

acid which is present in large amount in the kidneys of the new-born. We tested a number of fluids for the presence of iron with uniformly negative results.

The pocket size spectroscope was found of no value in detecting blood except when it was present in large amounts. We have not used the large size spectroscope in our work.

BILE

The nitric acid test was tried on a small series of cases and found negative. Realizing that the nitric acid test is not sufficiently sensitive for the detection of the bile, we later used the van den Bergh test [8] on seventy-three fluids. In none was there a direct positive reaction (in one to fifteen seconds). The indirect van den Bergh (fifteen seconds to one hour with a drop of alcohol added to the fluid) was faintly positive in five fluids, three of which were blood tinged. In sixty-eight fluids, the van den Bergh reaction was negative. The results of the van den Bergh test makes us believe that the yellow color so often obtained is not due to bile.

GLOBULIN

The Ross-Jones test was negative in eighty-six cases and positive in fourteen. The Pandy test was negative in forty-three and positive in fifty-seven. Of the twelve colorless fluids, three gave a positive Pandy reaction, seven a negative Pandy reaction and one was questionable. The Ross-Jones test was negative in all of the twelve colorless fluids. Of the clear yellow fluids, thirty-four gave a positive Pandy and twenty-nine a negative Pandy reaction. The Ross-Jones reaction was positive in nine fluids and negative in fifty-four.

One fluid that gave a 4 plus Wassermann test gave positive Ross-Jones and Pandy tests; another fluid with a 4 plus Wassermann reaction gave a positive Pandy but negative Ross-Jones reaction. One fluid that gave a 2 plus Wassermann test gave negative Ross-Jones and Pandy tests.

WASSERMANN TEST

The Wassermann test was positive in three fluids and negative in ninety-eight fluids. In one case in which the child's fluid showed a positive Wassermann reaction, the Wassermann reaction of the mother's blood was negative. Of three cases in which the maternal blood showed a positive Wassermann reaction, in only one case did the infant's fluid give a positive reaction.

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8. Van den Bergh, A. A. H.: Der Gallenfarbstoff im Blut, Leiden, 1918.

SUMMARY

We obtained cerebrospinal fluid from 100 new-born babies twenty-four times by spinal puncture, sixty-four times by cistern puncture and twelve times by combined spinal and cistern puncture.

We found the cistern puncture more reliable for the purpose of obtaining fluid.

When spinal puncture is performed, a dry tap is less likely to occur if the needle is introduced one or two spaces above the level of the crest of the ileum, and if a relatively short needle is used.

The amount of fluid obtained by spinal puncture varied in our cases from a few drops to 5 cc., with an average of 3 cc. The amount of fluid obtained by cistern puncture varied from 1.5 to 10 cc., with an average of 6 cc.

The color of the fluid in most cases was yellow. Twelve fluids were colorless; twenty-four blood tinged, and four distinctly bloody.

The yellow color of the fluid does not seem to be due to bile as the van den Bergh test was negative in all but five fluids, three of which were blood tinged. The benzidine test was positive in only twelve blood-tinged fluids, faintly positive in two blood-tinged fluids, and only barely positive in three clear yellow fluids.

It is possible that the yellow color of the fluid may be due to some intermediate blood compound which gives neither the benzidine nor the van den Bergh reactions.

The pressure of the fluid obtained by lumbar puncture varied from 1 to 6 mm. of mercury, with an average of 4.5 mm. In one case, the pressure was 20 mm. and in the other 16 mm.

In fluid obtained by cistern puncture, the pressure varied from 4 to 40 mm. of mercury, with an average pressure of 25 mm.

The rate of flow varied in spinal punctures from 1 drop per second to 1 drop every thirty-five seconds. The fluid in most cistern punctures spurted from the needle and kept flowing in a steady stream for a few seconds, after which it slowed down to 1 drop per second.

The cells varied from 6 per cubic millimeter to several hundred. Crenated cells were often found in fluids with a high cell count. There seemed to be no relation between the number of cells and the globulin content.

The Ross-Jones test was negative in eighty-six cases and positive in fourteen. The Pandy test was negative in forty-three and positive in fifty-seven. The Wassermann test was positive in three fluids and negative in ninety-eight fluids. The blood of the mother was positive in three cases. In only one of these cases was the cerebrospinal fluid of the

baby positive. In one case of a positive Wassermann test on the fluid, the Wassermann reaction of the mother's blood was negative.

In rare instances, cisterna puncture is accompanied by difficulties and even some danger.

Fresh blood in the spinal fluid is often the result of trauma, as well as of intracranial hemorrhage.

HEMATOPORPHYRINURIA

REPORT OF TWO CASES *

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Cases of hematoporphyrinuria following the ingestion of drugs, particularly sulphonal, are relatively common. There are, however, a small number of cases of so-called idiopathic hematoporphyrinuria reported chiefly in Germany and England. Two of the latter variety have recently been seen at this hospital. The findings agree so closely with descriptions by other authors that only a brief discussion will follow.

REPORTS OF CASES

CASE 1.—A colored boy, aged 3 years and 10 months, was admitted to the hospital Aug. 22, 1924, with the complaint of "abdominal pain." He died Jan. 22, 1925.

Family History.—The father, aged 28; the mother, aged 21, and one sister and one brother were all living and well.

Past History.—At the age of 22 months, two years before his present illness, the patient had been admitted to the Harriet Lane Home with an attack of acute diarrhea and bronchopneumonia. The urine at this time was entirely normal. He was discharged two and one-half weeks later. Except for this illness he had always been well.

Present Illness.—On July 12, six weeks prior to admission, the patient had complained of frequent attacks of abdominal pain, and of pain in the legs of such severity that walking was difficult. His mother had noticed that his urine was brownish red in color and that following urination the abdominal pain became less intense. His appetite was poor, and he was listless and generally fatigued. There was no history of vomiting, constipation or melena.

On July 20, one week later, the urine was clear, and the abdominal discomfort had disappeared. The pain in his legs persisted.

On August 22, one and one-half months after the onset, an attack similar to the first occurred, and he was admitted to the hospital.

Physical Examination (Dr. S. F. Ravenel).—The temperature was 101.6 F.; the weight 22½ pounds; pulse 130; respirations 30. There were evidences of old rickets, the sclerae were slightly jaundiced, the abdomen and lower extremities were somewhat tender on palpation and the knee jerks were active. No discoloration of the teeth was apparent. The spleen was not enlarged.

Laboratory Examinations.—The white blood count was 16,500; normal differential with 57 per cent polymorphonuclears; hemoglobin 70 per cent (Sahli). No stippling of red cells. The Wassermann reaction of the blood was negative. Tuberculin test (0.1 mg. intradermally) was negative. The urine was turbid and brown; albumin +++; acetone, urobilin, bile and guaiac tests were negative; there were a few white blood cells and granular casts.

A roentgenogram of the kidneys showed no evidence of stones.

On September 2, ten days later, there was marked weakness of the extremities with a frank right wrist drop, and a tendency toward foot drop. Fluid obtained from spinal puncture at this time had no increase in globulin, and the cell count was normal. The Wassermann reaction of the spinal fluid was negative; the

* Received for publication, April 27, 1926.

* From the Harriet Lane Home for Invalid Children, Johns Hopkins Hospital.

colloidal gold and mastic curves were normal. From September 2 to October 18, the dark color in the urine appeared intermittently for five weeks, and finally disappeared. The pains in his legs became less marked, and the strength returned to such an extent that he was able to crawl about. He was discharged on October 18, three months after admission, greatly improved. He walked shortly afterward, but the abdominal and urinary symptoms recurred at various intervals. On Jan. 22, 1925, three months after discharge, he had an attack similar to the preceding two, but did not seem very ill. Two days after the onset, death suddenly occurred. The clinical impression was hematoporphyrinuric polyneuritis and status thymicolymphaticus.

Necropsy.—All the viscera were darkly colored. The thymus was large and weighed 30 gm.; no signs of involution were found. The spleen was firm, dark red in color and definitely enlarged, weighing 220 gm. The capsule was smooth and Malpighian bodies were hardly visible. There were no alterations in the trabeculae and blood vessels, but an extraordinary packing of the pulp with red blood cells was noticed. There was no phagocytosis, and the iron reaction was negative. All the lymph nodes and Peyer's patches were hypertrophied, and there was a slight amount of phagocytosis of red cells in the lymph sinuses. The kidneys contained a large quantity of fat in the epithelium, and iron containing pigment was found in the convoluted tubules. The periportal capillaries of the liver were filled with red cells. There was no iron containing pigment in the liver. The bone marrow was hyperplastic, and suggested the possible formation of excessive amounts of blood. In the absence of any extensive phagocytosis, it seemed likely that a marked degree of blood destruction had occurred. No alterations of the peripheral nerves could be found. Spectroscopic examination of the urine obtained from the bladder at necropsy showed the typical bands of acid hematoporphyrin.

COMMENT

Cases of idiopathic hematoporphyrinuria with peripheral neuritis have been described by Harris,[1] Monro,[2] Barker and Estes,[3] Ascoli,[4] Schulte,[5] Harbitz,[6] Bachlechner,[7] Parsons,[8] Grund,[9] and Löffler.[10]

In general, the clinical picture consists of attacks of abdominal pain, vomiting, obstinate constipation and the excretion of a brownish red urine. The concurrent or subsequent peripheral neuritis not uncommonly results in a terminal ascending paralysis of the Landry type. The

1. Harris, W.: Toxic Polyneuritis, Brain **45**:415-433, 1922.
2. Monro, T. K.: On Hematoporphyrinuria not Due to Sulphonal, Quart. J. Med. **1**:49-52, 1907-1908.
3. Barker, L. F., and Estes, W. L., Jr.: Family Hematoporphyrinuria and Its Association with Chronic Gastroduodenal Dilatation, Peculiar Fits and Acute Polyneuritis, J. A. M. A. **59**:718-719 (Aug. 31) 1912.
4. Ascoli, V. R.: Il caso di ematoporfinuria, Policlinico (sez. prat.) **15**:84-85, 1908.
5. Schulte: Ueber Hämatophorphyrinurie, Deutsche Arch. f. klin. Med. **58**: 313-324, 1897.
6. Harbitz, F.: Hematoporphyrinuria as an Independent Disease ("Hematoporphyria") and as a Symptom of Liver Disease and Intoxications, Arch. Int. Med. **33**:632-642, 1924.
7. Bachlechner: Diss. Erlangen, 1914, quoted by Harris, W.: footnote 1.
8. Parsons, A. R.: Fatal case of Portwine-Colored Urine, Tr. Roy. Acad. Med. **26**:3, 1909; ibid., Lancet **1**:1112, 1909.
9. Grund, G.: Ueber Hämatoporphyrie mit Polyneuritis, Zentralbl. f. inn. Med. **40**:810-819, 1919.
10. Löffler, W.: Uber die bei akuter Porphyrinurie im Harn und Kot auftretenden Porphyrine, Biochem. Ztschr. **98**:105-115, 1919.

mortality is high and the prognosis is extremely variable. Cases with single or repeated attacks may be followed by complete recovery.

Hematoporphyrinuria with neurologic disturbances other than peripheral neuritis have been discussed by Ranking and Pardington,[11] Pal,[12] Brown and Williams,[13] Thornton,[14] Monro and Borland,[15] Günther,[16] Monro [2] and Harbitz.[6] Psychoses, epileptiform attacks and delirium are the most commonly mentioned symptoms.

Classification is exceedingly difficult, as both types closely simulate the clinical picture of toxic hematoporphyrinuria due to sulphonal. Keith Campbell [17] described a patient who had typical abdominal and neurologic symptoms following the use of only 30 grains of sulphonal. Günther has placed this in the idiopathic group, but as Campbell himself suggests, it may well represent a case of drug idiosyncrasy.

There are a few cases on record of asymptomatic hematoporphyrinuria. They have been for the most part unexpectedly discovered in patients suffering from other diseases. The best illustrations can be found in the articles of Neusser,[18] Nebelthau,[19] Arnold,[20] Calvert,[21] Snapper,[22] Dana,[23] Rodelius and Schumm,[24] and Sobernheim.[25]

The etiologic mechanism concerned in the production of hematoporphyrinuria is still entirely obscure. Neusser [18] believes that the pigment

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11. Ranking, J. E., and Pardington, G. L.: Two Cases of Haematoporphyrin in the Urine, Lancet **2**:607-609, 1890.

12. Pal, J.: Paroxysmale Hämatoporphyrinuria, Zentralbl. f. inn. Med. **24**:601-604, 1903.

13. Brown, W. L., and Williams, H. O.: Recurrent Haematoporphyrinuria with Toxic Symptoms not Due to Sulphonal, Lancet **1**:1105-1107, 1909.

14. Thornton, G. L.: A Case of Haematoporphyrinuria not Due to Sulphonal, Lancet **2**:888, 1904.

15. Monro, T. K., and Borland, H. H.: Haematoporphyrinuria not Due to Drugs, in a Patient Whose Urine Contained at Times Haemoglobin and at Times Sugar, Glasgow M. J. **75**:88-90, 1911.

16. Günther, H.: Ueber die akute Hämatoporphyrie, Deutsches Arch. f. klin. Med. **134**:257-297, 1920.

17. Campbell, K.: A Case of Haematoporphyrinuria, J. Ment. Sc. **44**:305-313, 1898.

18. Neusser, E.: Beitrag zur Lehre von den Harnfarbstoffen, K. Akad. d. Wissensch. Sitzungsb. Math. -naturw. Cl. Wien. **83**:536-560, 1881.

19. Nebelthau, E.: Beitrag zur Lehre vom Hämatoporphyrin des Harns. Ztschr. f. physiol. Chem. **27**:324-334, 1899.

20. Arnold, V.: Ein Fall von Hämatoporphyrinurie bei Abdominaltyphus, Ztschr. f. physiol. chem. **82**:172-174, 1912.

21. Calvert, J.: A Case of Haematoporphyrinuria not Due to Sulphonal, Tr. Clin. Soc. London **34**:41-45, 1901.

22. Snapper, I.: Porphyrinurie mit und ohne Koliken, Deutsche med. Wchnschr. **48**:619-621, 1922.

23. Dana, C. L.: The Metabolic Changes in Hematoporphyrinuria Not of Drug Origin, Am. J. M. Sc. **141**:247-253, 1911.

24. Rodelius, E., and Schumm, O.: Ueber Hämatoporphyrinogenausscheidung im Harn, Ztschr. f. urol. Chir. **3**:112-127, 1914.

25. Sobernheim, G.: Ein Beitrag zur Lehre von der Haematoporphyrinurie, Deutsche med. Wchnschr. **18**:566-567, 1892.

excretion results from abnormal reduction processes in the organism, which stop at a certain stage of the reduction after splitting iron from hematin (to form hematoporphyrin) and do not go far enough to create its last reduction product, namely, urobilin. Snapper [22] suggests that damage of the retroperitoneal nerve plexuses due to chronic poisoning is the primary lesion. Garrod [26] and others showed that the brown red

Fig. 1 (case 2).—Hydroa aestivale. Pigmentation and scarring of face and neck.

color of the urine is largely due to the presence of other abnormal pigments since the color persists after the removal of hematoporphyrin. This may mean a generalized disturbance of pigment metabolism. Garrod [26] attributes the cause to a perversion of hemoglobin catabolism, as he has observed patients excreting hematoporphyrin simultaneously

26. Garrod, A. E.: The Urinary Pigments in their Pathologic Aspects. Lancet **2**:1323-1331, 1900.

with a rise in hemoglobin and an increase in the total number of red cells. For this reason he is skeptical of the coexistence of hemolysis and hematoporphyrin. Unfortunately, no fragility tests were carried out on our patient. Brown and Williams [14] discuss the evidence of the theory of intestinal intoxication. Little aid comes from pathologic reports. Fatty degeneration of the viscera, particularly of the liver and the kidneys is commonly present. Hyperemia of the kidneys, hemorrhages in the intestinal mucosa and pigment deposits in the abdominal organs have frequently been found. In general, no pathologic lesion of a specific nature has been demonstrated.

Fig. 2 (case 2).—Showing distribution of lesions on the hands.

Case 2.—R. E., a white girl, aged 8 years and 2 months, was admitted to hospital May 11, 1924, and discharged May 18. Examination was made by Dr. J. A. V. Davies.

Family History.—The father, aged 44, the mother, aged 31, and two brothers, were all living and well. One grandmother and aunt have tuberculosis. There was no history of syphilis.

Past History.—The formation of clear vesicles on the dorsum of the hands was first noticed at the age of 5. These continued to recur and were followed by crusts and pigmentation. A few vesicles appeared on the chin. At the onset, a noticeable tanning of the face and hands occurred. This later spread up the arms and down the trunk to the waist-line. The mother also observed that the patient's urine was frequently pink in color, especially in the morning. Vesicle formation and the excretion of the abnormally colored urine were noted both in winter and in summer. The patient's general health was excellent.

Physical Examination.—Temperature, 99 F.; pulse, 108; respirations, 24; weight, 49 pounds; blood pressure, systolic 130; diastolic 30. She was apparently

normal except for the skin condition. The teeth were slightly stained but there was no actual discoloration. The spleen was not enlarged.

The dermatologic examination was made by Dr. I. R. Pels. His description may be summarized as follows: "There is a striking pigmentation of the face, neck, forearms and trunk extending downward to the waist-line. On the face, neck and arms are areas which have lost their pigment, and on palpation feel hard as if the subcutaneous tissue was infiltrated or sclerosed. These portions closely resemble scleroderma. On the fingers are vesicles and bullae in various stages of evolution. Scattered over the dorsum of the hands and neck are numerous crusted lesions. The eyebrows are sparse and the eyelashes irregular in size but there is no actual mutilation, as is often described in other cases."

Laboratory Examination.—Blood, white cell count 18,320 with an essentially normal differential count; hemoglobin, 78 per cent. There was a normal number of platelets. Red cell count, 4,768,000. There were no polychromasia.

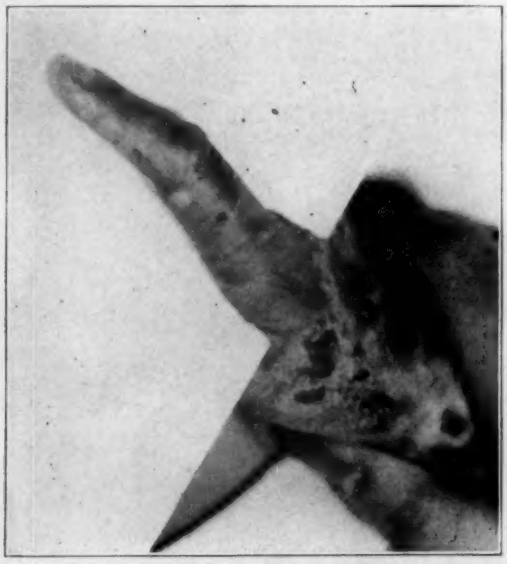

Fig. 3 (case 2).—Forefinger of right hand, showing typical bullae filled with clear fluid.

Tuberculin test (0.1 mg. intradermally) was negative. The urine was cloudy, Burgundy red and strongly acid, with a specific gravity of 1.028. There was no albumin in the night specimen; the day specimen was + +. There were numerous white blood cells but no casts. Sugar, guaiac, acetone and urobilin tests were negative. Spectroscopic examination showed large amounts of hematoporphyrin. Culture of bullae was negative; there was no growth after five days. The Wassermann reaction of the blood was negative. Coagulation time was three minutes and fifty seconds.

Protein sensitization tests (twenty-five various proteins used) were all negative. The impression was hydroa-estivale with hematoporphyrinuria; orthostatic albuminuria.

The child was visited one and one-half years later at her home in Tanneytown, Maryland. No vesicle formation had occurred for over a year. The scars had largely disappeared and the previously affected skin was much softer. The eyebrows had entirely returned, and only the extensive pigmentation of the upper half of the body remained. The urine has continued to be dark brown for days at a time.

COMMENT

Similar cases are recorded by McCall Anderson,[27] Harris,[28] MacMunn,[29] Schultz,[30] Vollmer,[31] Linser,[32] Gross,[33] Mackey and Garrod,[34] Ashby,[35] and Sato and Takahashi.[36]

In general, the attacks occur in summer following exposure to the sun's rays. There is often a prodromal period of itching followed by vesicle formation and later scarring. The scleroderma which was so prominent a feature in our case has been often described, and seems to be a result of repeated scarring. The attack lasts only a few days, and is usually associated with the excretion of a reddish urine, rich in hematoporphyrin. The onset is early in life, and the heredofamilial factor has been frequently emphasized. Pink or purple colored teeth were present in some of the cases referred to in the foregoing. Enlargement of the spleen is less commonly mentioned. A brownish discoloration of the skeletal structures is the most consistent necropsy finding. We could obtain no history from our patient of a direct relation between the appearance of the attacks and the exposure to light. That such a close relationship exists, however, is evident clinically from the histories of other cases, and experimentally from the work of Meyer-Betz [37] and others.

The most comprehensive review of the entire subject is contained in Günther's excellent monograph.[38]

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27. McCall Anderson, T.: Hydroa Aestivale in Two Brothers, Complicated with the Presence of Haematoporphyrin in the Urine, Brit. J. Dermat. **10**:1-4, 1898.

28. Harris, D. F.: Haematoporphyminuria and Its Relations to the Source of Urobilin, J. Anat. & Physiol. **31**:383-391, 1897.

29. MacMunn: Pigments of Urine, J. Physiol. **11**:13-14, 1890.

30. Schultz, J. H.: Ein Fall von Pemphigus leprosus, complicirt durch Lepra visceralis. Inaug. -Diss. Greifswald, 1874. Quoted by Baumstark in Pflügers Arch. f. d. ges. Physiol. **9**:568, 1874.

31. Vollmer, E.: Ueber hereditäre Syphilis und Haematoporphyrinurie, Arch. f. Dermat. u. Syph. **65**:221-234, 1903.

32. Linser, P.: Ueber den Zusammenhang zwischen Hydroa aestivale und Hämatoporphyrinurie, Arch. f. Dermat. u. Syph. **79**:251-256, 1906.

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34. Mackey, L., and Garrod, A. E.: On Congenital Porphyrinuria Associated with Hydroa Aestivale and Pink Teeth, Quart. J. Med. **15**:319-330, 1921-1922.

35. Ashby, H. T.: A Case of Haemotoporphyria Congenita (Congenital Porphyrinuria), Brit. M. J. **2**:803, 1924.

36. Sato, A., and Takahashi, H.: A New Form of Congenital Hematoporphyria, Am. J. Dis. Child. (To be published.)

37. Meyer-Betz, F.: Untersuchungen über die biologische (photodynamische) Wirkung des Hämatoporphyrins und anderer Derivate des Blut- und Gallenfarbstoffes, Deutsche Arch. f. klin. Med. **112**:476-503, 1913.

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PELLAGRA

REPORT OF A CASE IN A CHILD AGED SEVENTEEN MONTHS

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The following case is reported as of interest because of the relatively infrequent occurrence of pellagra in the District of Columbia, the rarity of the disease in children under 2 years of age, the seemingly quick response to treatment of an attack of more than average severity, and, finally, because of the favorable progress and outcome of the case.

REPORT OF CASE

History.—C., a colored boy, was born March 22, 1924. The father and mother are alive and well. The mother has had two pregnancies, the first resulting in a child who is now 3 years old and well; the second, the infant in question. There was no history of eruptive disease in any other member of the family.

The baby was born at term; labor was normal. The birth weight is unknown, but is believed to have been about 7 pounds (3.2 Kg.). No neonatal abnormalities were noted.

According to the mother's statements: The child was born on the outskirts of Anacosta, D. C., had never been out of the District of Columbia, and prior to the present illness had never been sick. He was breastfed exclusively for six months. No system of feeding had been used; both breasts were given at each feeding, and he was fed whenever the mother thought he was hungry: about once every hour during the day, less frequently at night. Chicken, and sometimes beef, broth was given after the child was 6 months old, and after the first year soft boiled egg and cooked potato had been added. Cow's milk had not been given, and the child seldom had vegetables.

History of the mother's diet during the period of lactation was not obtained.

Present Illness.—About Sept. 1, 1925, when, according to the mother, the child was "cutting teeth," he began to lose weight and she noticed swelling of the feet. An eruption, which was said to have started the latter part of November, began with an area under the knee about the size of the head of a pin and spread. The baby vomited only when given something he did not appear to want. The bowels moved on an average of three or four times daily; the stools were loose but not watery, and the odor was reported to be foul.

Orange juice and broth were said to have been given since the middle of November, but no milk. The child grew gradually worse, and was brought to the dispensary of the Children's Hospital, November 30.

Physical Examination.—The child was in the dorsal decubitus position. He was apathetic, except on handling, when he became fretful. A widely distributed pigmented eruption was present; both feet were edematous. The nutrition was very poor and the child appeared anemic. The height was 30 inches, and the weight was 15 pounds (6.8 Kg.).

There were several brown, pigmented spots on the scalp behind the right ear, a dry pigmented scaly eruption on the left side of the head at the hairline and on the right side just above the brow, and pigmentation with some scaling of the

* Received for publication, May 14, 1926.

* From the Medical Service of Children's Hospital.

superior edge of the left ear and, to a lesser degree, of the right ear. The skin under the chin and on the chest and shoulders was dry and scaly. There was some pigmentation at the base of the neck posteriorly, and a dry pigmented eruption on the backs of both hands which extended for about 1 inch on the left wrist anteriorly and posteriorly, and on the right arm as far as and including the elbow. Evidence of desquamation of both wrists and the back of the right hand was present. There was pigmentation of the dorsum of the penis and of the scrotum extending to the perineum, and a pigmented eruption on the inner and outer aspects of the right thigh, extending through the popliteal space for a short distance on the right calf. On the right side, desquamation occurred on the thigh and buttock, leaving the skin shiny and wrinkled.

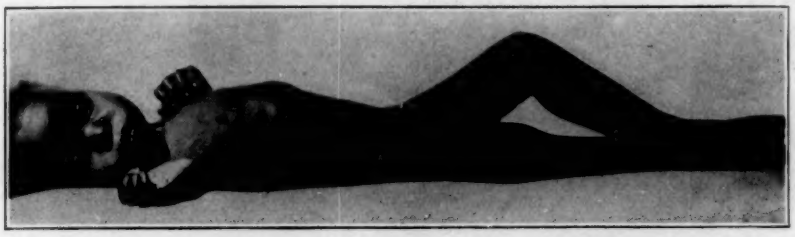

Fig. 1.—Emaciation. Eruption on thighs; anterior view.

Fig. 2.—Eruption on buttocks and thighs; posterior view.

There were small patches of lighter colored pigmentation on the dorsum of both feet; the toes of both feet were the site of a purplish discoloration with a suggestion of bleb formation. A bleb on the dorsum of the second toe of the right foot was broken, leaving a raw surface; there was desquamation of the skin of the soles of both feet. There were small pigmented spots in the lumbar and sacral regions extending over the coccyx.

The head was normal in size and shape; the fontanels were closed. The thorax was bony and the abdomen somewhat tense. The upper extremities and the thighs were flabby and emaciated; the calves appeared larger in proportion. There was some bowing anteriorly of both tibiae. The feet were markedly edematous, especially the left one; this edema affected particularly the dorsum of the feet and extended past the ankle; there was pitting on pressure. The spine was prominent. Tissue turgor generally was poor. The superficial lymphatics were not palpable.

3.—Edema of feet; eruption at base of toes.

Fig. 4.—Pigmentation and desquamation on dorsum of hands and wrists, and on face.

The eyes appeared normal except that the expression was dull. The lips, particularly the lower one, appeared smooth, shiny and somewhat brighter red than would normally be expected; the corners were slightly fissured. The mucous membrane of the mouth was in fairly good condition; that of the right cheek was somewhat overred. There were sixteen teeth, which were in poor condition, especially the four upper incisors, which appeared friable and worn almost to the gum line. The gums were inflamed and beefy red. The tongue was slightly coated except at the tip and margins which appeared red. The fauces, pharynx and tonsils were about normal.

The heart action was weak and somewhat irregular; there were no adventitious sounds and the rate was 96. The rectal temperature was 99 F.

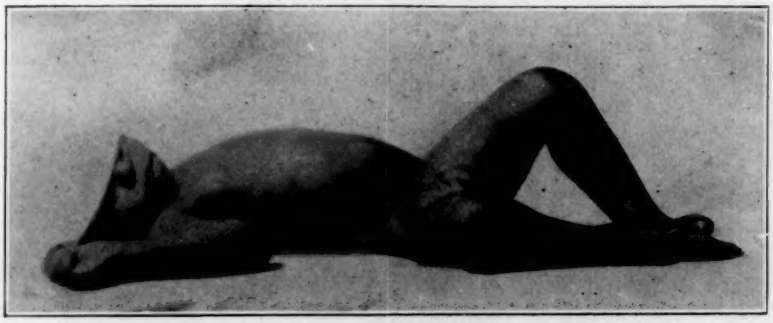

Fig. 5.—Improved nutritional state. No eruption; anterior view.

Fig. 6.—Improved nutritional state. No eruption; posterior view.

The lungs were clear and the respiratory rate was rather slow. The liver and spleen were not palpable.

Phimosis was present; the testes could not be palpated in the scrotum.

The patellar reflexes were equal but sluggish.

Figures 1, 2, 3 and 4 illustrate the appearance of the patient shortly after admission.

On December 1, the patient was seen by Dr. Joseph Goldberger, who confirmed the diagnosis of pellagra and expressed the opinion that the edema of the feet was probably an indication of associated beriberi. Dr. Goldberger suggested that yeast in the form of yeast vitamin powder (Harris) be given in solution, in addition to a diet of fresh milk, orange juice and beef juice.

On December 17, Dr. D. D. V. Stuart made a neurologic examination. His impression was that the patient probably had a recovering peripheral polyneuritis.

Laboratory Findings.—Repeated urinalysis revealed a persistent trace of albumin with the presence of finely granular casts, which later cleared up. A culture of the feces revealed *B. coli.*

Examination of the blood showed 60 per cent hemoglobin; 4,500,000 erythrocytes, and 8,200 leukocytes per cubic millimeter. The differential leukocyte count was normal. The Wassermann and tuberculin reactions were negative.

Roentgenograms of the long bones, unfortunately delayed until after the child was discharged from the hospital, gave definite evidence of healed rickets of a moderately severe type.

Treatment.—Treatment was dietary, and included 1 Gm. of yeast vitamin powder (Harris) in solution in 1 teaspoonful of water three times a day, fresh cow's milk, expressed beef juice and orange juice. Later, cereal jellies, scraped

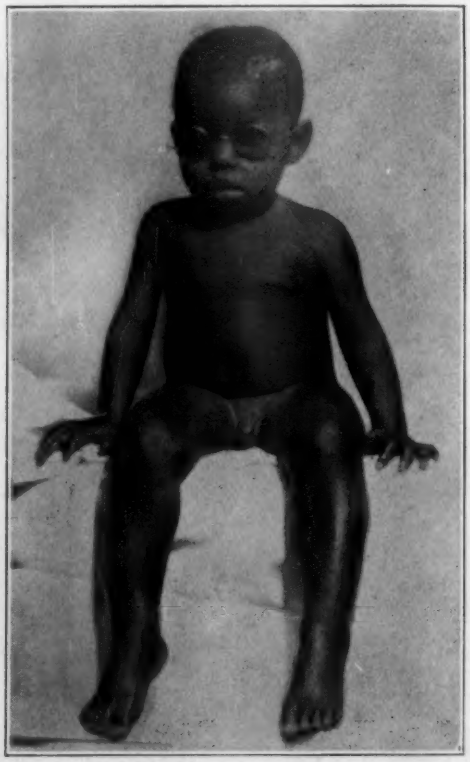

Fig. 7.—Improved nutritional state. Edema of feet has disappeared; disappearance of eruption.

beef cake, and cod liver oil were added. After one week the yeast vitamin powder was supplanted by one commercial yeast cake, emulsified in water three times a day. Later, vegetables were added to the diet. After about one month's residence in the hospital, the child was taking the usual diet of a 2 year old child, with the addition of three yeast cakes a day.

Clinical Course.—The child began to gain weight shortly after admission, and with the exception of a loss noted as the edema of the extremities disappeared, continued to gain until he weighed 21 pounds (9.5 Kg.) on discharge from the

hospital on Feb. 6, 1926. The patient had thus increased about 40 per cent in weight.

The eruption gradually disappeared. No new areas were observed, except one on the dorsum of the great toe of the right foot, which became the site of a large bleb. Desquamation progressed for several weeks. The edema of the feet began to disappear shortly after admission, and was entirely gone in about two weeks.

The mouth, gums and lips became normal slowly.

There were from two to five very foul loose stools a day for one month after admission. Later the number was reduced and they became more normal.

The mental condition of the child became brighter, and about three weeks after admission he would smile. Within the next three weeks he walked and was quite active.

Recovery was uneventful, except for a bilateral otitis media due to *M. catarrhalis*, which cleared up without difficulty.

Figures 5, 6 and 7 illustrate the appearance of the patient after discharge.

COMMENT

Although the child was 20 months of age when first observed, the disease, from its state of development, may be fairly assumed to have been in existence for three months prior to admission to the hospital.

The sporadic nature of this condition would be an evidence of the dietary nature of the disease, as against the possibility of infection as an etiologic factor.

The presence of pellagra, rickets, and possibly beriberi (all nutritional diseases), in the same patient, is interesting.

The appearance of the mouth, gums and teeth in this patient was not unlike that seen in scurvy. It is possible that some cases of pellagra may be diagnosed as scurvy with an eruption.

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A COMPREHENSIVE PLAN OF TREATMENT FOR THE SO-CALLED INTESTINAL INTOXICATION OF INFANTS*

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Intestinal intoxication, while perhaps less frequently seen now than formerly, is still not an uncommon condition, and one greatly feared because of incomplete knowledge in regard to pathogenesis and inadequate measures of treatment. The clinical picture is well known, and is in many respects similar to that reported in inanition fever of the newborn,[1] Asiatic cholera,[2] severe burns,[3] high intestinal obstruction,[4] traumatic and histamine shock,[5] lethal war-gas poisoning,[6] certain cases of influenza[7] and induced dehydration in animals.[8] The basis for correspondence in symptoms is probably to be found in increased blood concentration, a condition common to all of these otherwise unrelated maladies. Since morbid states such as these, wholly diverse in etiology, may present a similar clinical picture, pediatricians ought to recognize the probability that intestinal intoxication, so-called, is but a symptom-

* Received for publication, July 9, 1926.

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* Attempt is made to give, not a bibliography of intestinal intoxication, but only the authorities for certain statements. An extensive bibliography may be obtained in the articles cited.

1. Bakwin, H., and Goss, C.: Dehydration Fever in New-Borns, Am. J. Dis. Child. **24**:497 and 508 (Dec.) 1922.

2. Heubner, O.: Lehrbuch der Kinderheilkunde, 1. Band, Dritte Umgearbeitete Auflage, Leipzig, Johann Ambrosius Barth, 1911. Reiss, E.: Untersuchungen der Blutkonzentration des Säuglings, Jahrb. f. Kinderh. **70**:311, 1909.

3. Underhill, F. P.; Carrington, G. L.; Kapsinow, R., and Pack, G. T.: Blood Concentration Changes in Extensive Superficial Burns, and Their Significance for Systemic Treatment, Arch. Int. Med. **32**:31 (July) 1923.

4. Whipple, G. H., and Cooke, J. V.: Proteose Intoxications and Injury of Body Protein. I. Metabolism of Fasting Dogs Following Proteose Injections, J. Exper. Med. **25**:461 (March) 1917. II. (with T. Stearns.) The Metabolism of Dogs with Duodenal Obstruction and Isolated Loops of Intestine, ibid., p. 479.

5. Dale, et al.: Traumatic Toxaemia as a Factor in Shock, Medical Research Committee, Special Report Series No. 26, London, His Majesty's Stationery Office, 1919. Keith, N. M.: Blood Volume Changes in Wound Shock and Primary Haemorrhage, Medical Research Committee, Special Report Series No. 27, London, His Majesty's Stationery Office, 1919.

6. Underhill, F. P.: The Physiology and Experimental Treatment of Poisoning with Lethal Gases, Arch. Int. Med. **23**:753 (June) 1919.

7. Underhill, F. P., and Ringer, M.: Blood Concentration Changes in Influenza, J. A. M. A. **75**:1531 (Dec. 4) 1920.

8. Keith, N. M.: Experimental Dehydration: Changes in Blood Composition and Body Temperature, Am. J. Physiol. **68**:80 (March) 1924.

complex dependent largely on abnormal concentration of the blood, a condition which may be precipitated in babies in a variety of ways and under diverse circumstances.

In the treatment of intoxication, it seemed to us that if all measures of proved worth were assembled and coordinated for concerted use at the outset of treatment, each unit supporting and reinforcing others, results ought to be better than with isolated procedures more or less unsystematically carried out. Such an organization into a comprehen-

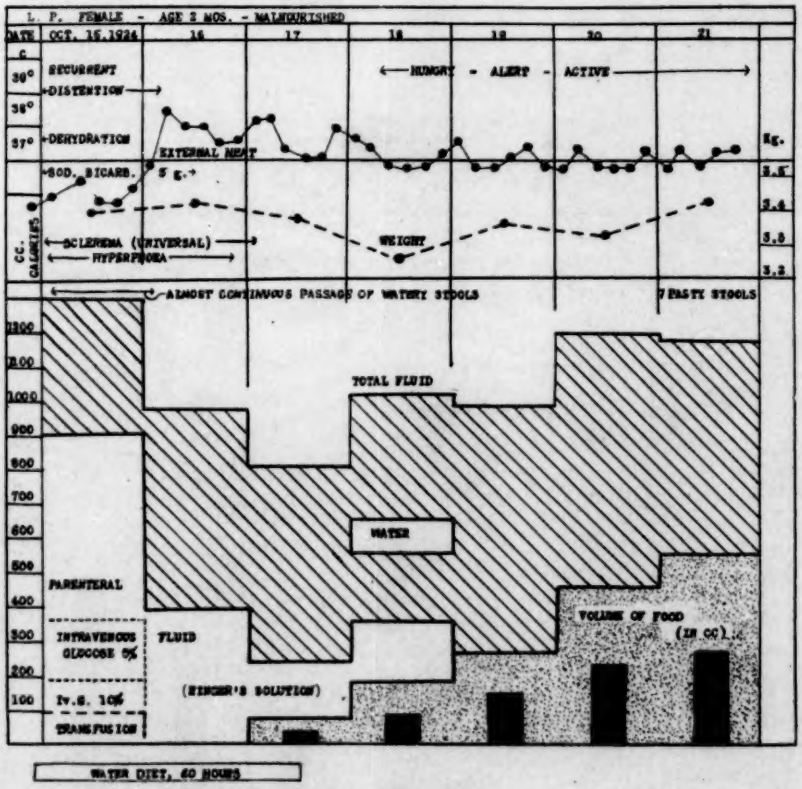

Chart 1.—Baby sent in as case of "meningitis"; weaned at 5 weeks; put on dilute unboiled cow's milk mixture; developed diarrhea. Vomiting for past week; refusal of food for three days. Moderately malnourished, extremely dehydrated infant; hyperpneic, slate-gray color, staring eyes, coma, no cry; universal sclerema; no evidences of infection. Outlook exceedingly grave for first forty-eight hours in hospital, stools innumerable; then baby became alert and able to cry fairly vigorously; sclerema gradually disappeared, watery diarrhea ceased; satisfactory convalescence. Food given at end of sixty-two hours of water diet; caloric intake gradually increased from 7 per kilogram on the first day of feeding to 107 per kilogram on the tenth day; ten feedings per twenty-four hours for six days and then eight. Feedings at first, skimmed milk with 2 per cent added glucose (1 cc. = 0.5 calories).

sive plan of treatment of therapeutic measures, no one of which is original with us, has been attempted in this clinic. The results have been so favorable that members of the resident staff have ceased to dread cases of intoxication as they did formerly, when a more or less haphazard, symptomatic treatment was employed (chart 5).

We believe the essential points in the treatment of intestinal intoxication center about four major procedures, namely, the administration of fluids, the transfusion of blood, the withholding of food for a period of time, and the administration of food at the end of the period of starvation in gradually increasing amounts (charts 1, 2, 3, 4 and 5).

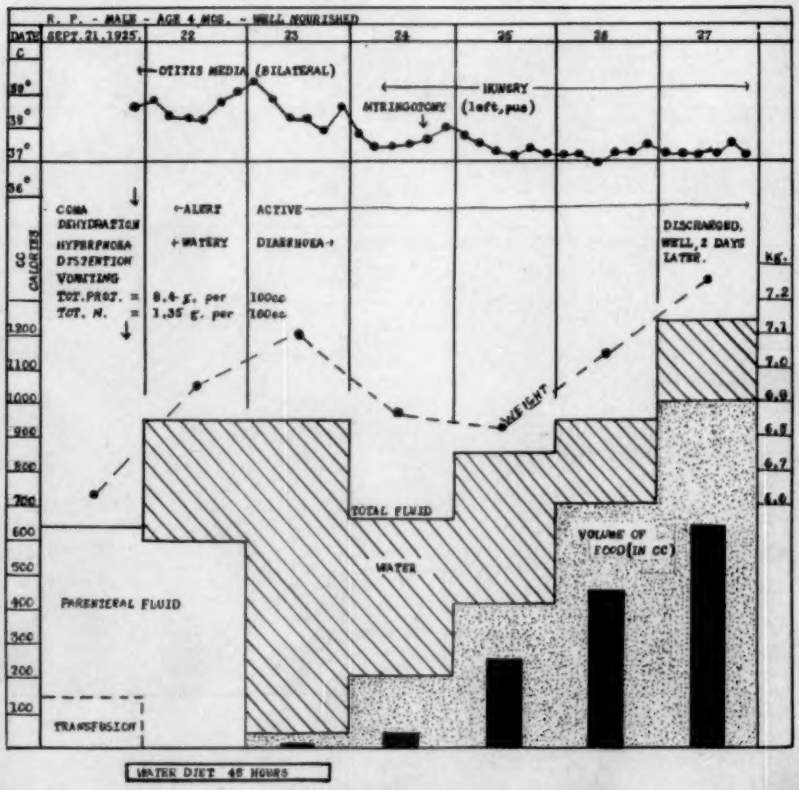

Chart 2.—The infant referred to in this chart was breast fed one month, then given very dilute sweetened condensed milk mixture in large amounts; no orange juice or cod liver oil. Eight days before admission the patient had severe diarrhea, a watery green movement "every half-hour"; later it began to refuse food and on the day before admission vomited and became "feverish." On admission, there was little diarrhea, but the child was exceedingly ill; recovery was scarcely hoped for; the extremities were cold; the face ashen gray, with hyperpnea and otitis media present. The first feedings were skimmed lactic milk (fermented) with 3 per cent barley flour (1 cc. = 0.6 calories). The case illustrates a quick "comeback" of well nourished child, even when desperately and apparently hopelessly ill.

THE ADMINISTRATION OF FLUIDS

There is no doubt that dehydration[9] plays a most important, if not primary rôle, in the production of the toxic symptoms often associated with the severe diarrheas of infants. Depletion of the body fluids[10] and the consequent increase in the concentration of the blood bring about many derangements in metabolism and vital functions.[11] It is natural, therefore, that first consideration in treatment should be given to measures which will remedy this condition. The fluid intake should be increased by giving physiologic sodium chloride solution parenterally, citrated blood intravenously, and water orally. We have availed ourselves of most of the methods of administering fluids—by mouth, nasal drip, hypodermoclysis and intraperitoneal injections; it is rarely possible to give fluid successfully to these patients by rectum. Our first procedure usually is to give the patient an injection of Ringer's solution intraperitoneally.[12] The use of this method for the first administration of fluid seems preferable to intravenous injection, even in very severe cases, because a larger quantity of fluid can be given intraperitoneally than intravenously and there is more gradual restoration of blood volume. If the patient is moribund, it is perhaps desirable to give 50 or 75 cc. of fluid intravenously (isotonic glucose solution) first and then, if the infant rallies, Ringer's solution intraperitoneally. The amount of fluid given intraperitoneally is determined by the capacity of the abdominal

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9. It should be emphasized, as the work of Gamble (J. Clin. Invest. **1**:403 [June 20] 1925) and of Underhill has clearly done, that although in this connection the words "dehydration" (removal of water) and "anhydremia" (lack of water in the blood) are used, the terms are inaccurate. They are supposed to denote bodily states which are often dependent on loss of many substances (salts, proteins, etc.) in abnormal amounts in addition to water itself.

10. Depletion of the body fluids may be brought about not in one, but in many ways; a variety of factors are involved, one or several of which may be operative in a given case. Usually, fluid output is erroneously thought of only in terms of the water content of urine and feces; the water lost in the breath and sweat is of importance in the body economy and may often play the significant rôle, at present unappraised, in the production of dehydration in certain patients, Marfan and Dorlencourt (Nourrisson **10**:173 [May] 1922) have shown that the amount of water lost in the breath in infants with intestinal intoxication may be 50 per cent greater than in normal infants.

11. Schloss, O. M., and Stetson, R. E.: The Occurrence of Acidosis with Severe Diarrhea, Am. J. Dis. Child. **13**:218 (March) 1917; Intestinal Intoxication in Infants, ibid. **15**:165 (March) 1918. Marriott, W. M.: Some Phases of the Pathology of Nutrition in Infancy, Am. J. Dis. Child. **20**:461 (Dec.) 1920; Anhydremia, Physiol. Rev. **3**:275 (April) 1923. Howland, J., and Marriott, W. M.: Acidosis Occurring with Diarrhea, Am. J. Dis. Child. **11**:309, 1916. Clausen, S. W.: Anhydremic Acidosis Due to Lactic Acid, Am. J. Dis. Child. **29**:761 (June) 1925. Rountree, L. G.: The Water Balance of the Body, Physiol. Rev. **2**:116 (Jan.) 1922.

12. Blackfan, K. D., and Maxcy, K. F.: The Intraperitoneal Injection of Saline Solution, Am. J. Dis. Child. **15**:19, 1918.

cavity to receive the fluid without distention; from 150 to 350 cc. may be given in this way at one time. Usually, intraperitoneal injection is followed by hypodermoclysis; the amount of fluid which can be given in this way is usually less than can be given into the peritoneal cavity. If the patient is distended, hypodermoclysis only is used. I have observed only one serious accident resulting from an intraperitoneal injection; it is undoubtedly our most satisfactory method of administering fluids to infants with intoxication. It must be emphasized, however, that this procedure should never be employed when the patient is distended. Most infants with intoxication have scaphoid abdomens, but this is by no means the invariable rule. Needless to say, in injecting fluid into the peritoneal cavity, careful technic must be observed.

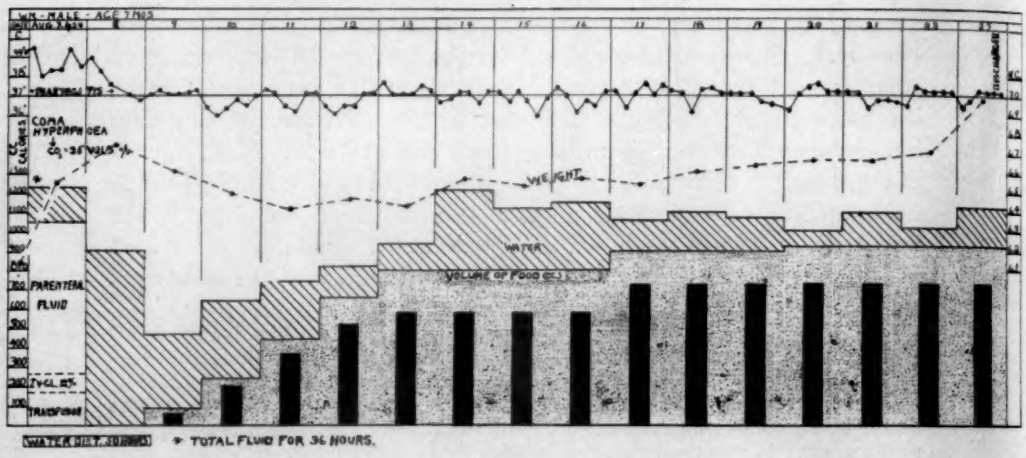

Chart 3.—Baby suddenly weaned because of mother's death; developed pharyngitis and parenteral diarrhea. On admission, in the evening, baby alert and "playful"; regarded as mild case of diarrhea; treated by parenteral fluids and starvation. Twelve hours after admission, baby very gravely ill. Treatment is given on the chart, which shows the entire course in hospital. The patient was discharged on the eighteenth day weighing 526 Gm. above admission weight. The low fluid intake on the third, fourth and fifth days is inexplicable and seems unwarranted. Feedings at first were skimmed lactic milk (fermented) with 7 per cent dextrimaltose and 3 per cent barley flour (1 cc. = 0.8 calories). The star indicates the total amount of fluid for thirty-six hours. This case illustrates (1) the impossibility of foretelling the potential seriousness of dehydration associated with diarrhea and vomiting, and the ease with which a mistaken judgment is made; (2) the relatively good prognosis which may be given in a case of severe intoxication if it occurs in a previously healthy child.

After the patient has received fluid parenterally, transfusion is performed. When these treatments have been carried out the patient is usually so much improved that consideration may be given to the administration of water by mouth. The amount and manner of giving water is determined largely by trial and error. Our practice is to begin by

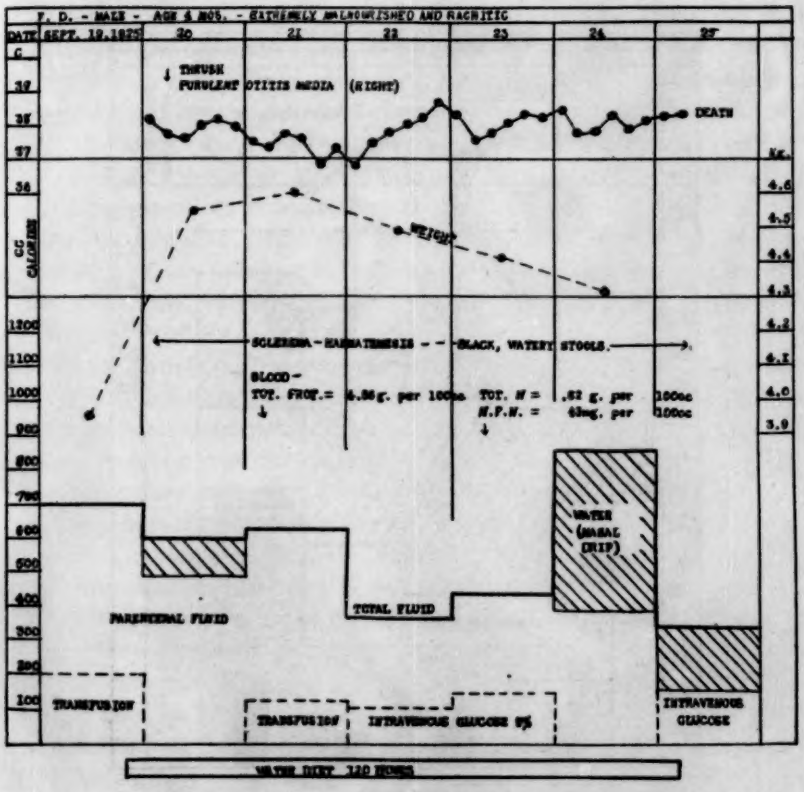

Chart 4.—The infant was breast fed for three months; then was given undiluted, unboiled cow's milk, in unknown quantities, every two hours. One week before admission, the infant began to vomit "everything," and was put on barley water, which was also vomited. The stools were loose, frequent and watery. The patient was desperately sick on admission; was atrophic, extremely rachitic, and of ashen color; universal sclerema, hyperpnea, cold extremities, a feeble cry, a relatively slow (80) and feeble heart action, and purulent otitis media were present. The vomitus was coffee ground in color; the stools were black and fluid. There was very little improvement in any way during the stay in hospital.

From the outset this case seemed hopeless because of the extreme emaciation, rickets, infection and the persistent melena. There was little or no response to treatment, which included a very large transfusion on admission (50 cc. per kilogram of body weight). This is the type of case in which treatment is often inadequate. Although still toxic, this child would have received food had it not been for the repeated hematemesis. Blood protein was low in spite of severe dehydration because of the patient's atrophied condition; hence, the danger of using protein concentration as the index, in all cases, of degree of dehydration.

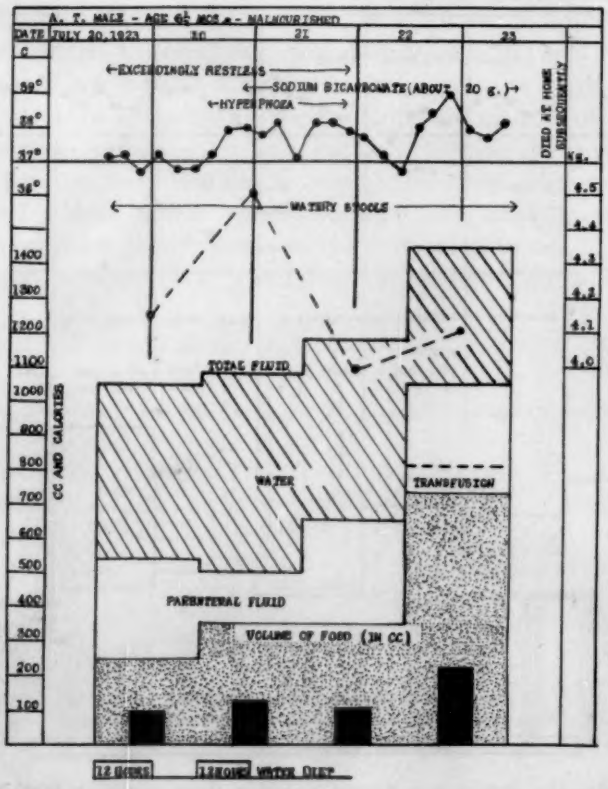

Chart 5.—An infant, breast fed for two months, was then given large amounts of dilute cow's milk (unboiled) mixture. Vomiting large amounts was present for two months; the stools were frequent, loose and watery; the child was losing weight. There was subcutaneous fat; the infant was markedly dehydrated, very restless, hyperpneic and rachitic. The stools were very watery; there was no vomiting while in hospital. The patient became steadily worse; the acidosis improved; alveolar air 40 mm. carbon dioxide tension eighteen hours before discharge. The child was discharged against advice on the fifth day, and died at home.

The chart illustrates the type of treatment which is not advised. The patient should have been given a transfusion of at least 125 cc. of blood on admission, not with 65 cc. four days later. Food should have been withheld when toxic symptoms were obviously present. (Feedings were skimmed lactic milk and rice gruel.) Alkalis should not have been given in small doses at frequent intervals over a long period of time; probably the patient should have received sedatives. A delay in paracentesis is not justified in cases of this type.

giving 10, 20 or 30 cc. of ice cold water at fifteen or thirty minute intervals. If vomiting does not occur, or is only very slight in amount, the quantity of water may be increased and the interval lengthened. If the patient is hyperirritable and is disturbed by attempts to administer water, it may be best to give a sedative and discontinue all treatment for six or eight hours; under these circumstances this is the best practice in view of the fact that parenteral saline and blood have already been given. It is desirable, however, to give patients with intoxication just as much water by mouth as possible during the first forty-eight hours. Even when the intake by mouth is great, the parenteral administration of fluid usually has to be employed once or twice a day during this period and, as a rule, cannot be dispensed with entirely, even in the most favorable cases, for several days.

If the patient vomits water in considerable amounts, it may be well to try lavage with a 1 per cent solution of sodium bicarbonate; then ice-water in small amounts at frequent intervals may often be given successfully. Another procedure is to give water by the continuous drip method through a nasal catheter. (I do not know who is responsible for introducing this procedure into pediatric practice; I first saw it employed by Dr. H. G. Stewart, formerly of the Johns Hopkins Hospital. It is important that the catheter be soft, that it extend into the esophagus only about half way to the cardia, and that the catheter be in place not longer than two hours with free intervals of at least that length.) If success does not attend these measures, as in rare instances is the case, lavage may be repeated, or all attempts to give fluid by mouth may be discontinued for three or four hours. As a matter of fact, however, if vomiting has occurred, as it often has in these patients, it usually ceases after fluid has been given parenterally; this result may be expected in most cases even when there has been hematemesis. Many severely dehydrated infants, particularly those who are greatly malnourished, vomit changed blood and pass blood in their stools (chart 4). Whether this is due to so-called "gastric erosions" or to simple passage of red cells through mucous membranes whose circulation is defective (or, in the case of atrophic infants, possibly to actual gastric or duodenal ulcers), I do not know, but after the dehydration is overcome, the bleeding often ceases; if it does not, the prognosis is aggravated. Dogs which are the subject of induced dehydration often pass mucus and blood in their stools.[8]

We have pushed fluid administration in these cases until the staff find that no clinical evidences of dehydration exist, or, rarely, until slight edema is manifest. One is guided in determining the time for forcing fluids and the extent to which they should be forced by the condition of the skin as regards turgor and elasticity, of the mucous mem-

branes of the mouth and eyes as regards moistness and by the amount of urine. The weight curve is a further guide, for without treatment these infants lose weight rapidly. I am convinced, however, that infants may sometimes show severe constitutional reactions because of dehydration when the objective signs of that condition are exceedingly slight.

The amount of fluid which must be given is, of course, subject to great variation. We have found that few children seem to require less than one liter daily; the maximum amount administered to any of our patients per day was two liters; the usual amount was about 1,200 cc. On the whole, it may be questioned whether the administration of fluids to infants with dehydration is usually pressed to the optimum point; the error is, I believe, more frequently on the side of stopping short of it rather than of overstepping it. One must take note of the extreme instability in water retention shown by some patients with intestinal intoxication. The tissues of such infants are lacking in turgor and elasticity and yet, paradoxically, fluid given to them is not retained. This phenomenon of instability in the water content of the tissues is an ominous sign; patients exhibiting it often do not respond satisfactorily to treatment and many of them die. Transfusion often greatly increases the ability of the tissues to retain water but, so long as these patients are dehydrated, we cannot perceive that it is harmful; on the contrary, it is temporarily helpful to give large quantities of fluid even though little is retained. One need not fear the development of so-called "water intoxication" when Ringer's solution or physiologic sodium chloride is given parenterally; Underhill [13] has shown that "water intoxication" is due to a washing out of chlorides from the body and does not occur when the body is flooded, not with water, but with physiologic sodium chloride.

Bakwin, Morris and Southworth [14] state that in dehydration the effect of physiologic sodium chloride solution given subcutaneously or intraperitoneally on "the temperature and blood concentration was neither so marked nor so regular as after water by mouth." It is not possible, however, in most cases of intoxication to give fluid orally in adequate amounts, even if vomiting is not present; it is necessary that fluids in large quantities be supplied quickly. Fluids given parenterally meet these requirements, and with advantage to the patient, if one may judge from the improvement which greatly dehydrated infants make after such treatment. Ringer's solution or physiologic sodium chloride may be eliminated fairly quickly from the body, but an adequate amount

13. Underhill, F. P., and Sallick, M. A.: On the Mechanism of Water Intoxication, J. Biol. Chem. **63**:61 (Feb.) 1925.

14. Bakwin, H.; Morris, R. B., and Southworth, J. D.: The Effect of Fluid on the Temperature and Blood Concentration in the New-Born with Fever, Am. J. Dis. Child. **27**:578 (June) 1924.

is certainly retained for a sufficient time to benefit the organism. During this period of improvement, a transfusion is done and the administration of water by mouth is begun; the favorable course initiated by the sodium chloride is thus usually maintained and continued. Repetitions of injections of parenteral fluid are not attended by the dramatically favorable responses which usually follow the initial two or three treatments. The most effective solution of electrolytes to administer to patients with intoxication is not known; some information might be obtainable for each case by a metabolic study but such study cannot be carried out. It is quite possible that the same solution may be equally effective for all patients with dehydration; if this be not the case, one can only hope that a transfusion of blood will make restitution, in part at least, for the inadequacies of the more simple fluids now used. In intraperitoneal and subcutaneous injections of fluid we have used Ringer's solution because in the presence of partial demineralization, a solution more complete in electrolytes than physiologic sodium chloride seems theoretically indicated. However, I have never observed clinically any superiority of Ringer's solution over physiologic sodium chloride solution. We have also, at times, given 5 and 10 per cent glucose solutions subcutaneously. The sites of injection have often become painful, and have sometimes shown ecchymoses and inflammation; this has been particularly common when repeated treatments have been given to the same patient. Furthermore, absorption from the tissues has often been slow. Not all observers, however, have had these experiences.

In some patients, after the introduction of fluid intraperitoneally and subcutaneously, intravenous injection of a 10, 15 or sometimes 20 per cent [15] glucose solution has been given. These solutions are hypertonic and were used only after subcutaneous or intraperitoneal fluid had been administered. Usually, from 15 to 25 cc. of glucose solution per kilogram of body weight was given intravenously in a period of about ten or fifteen minutes.

The theoretic value [15] of a glucose solution to patients with intoxication may be summarized as follows: If properly prepared it is nontoxic; it increases the fluid content of the blood; it supplies energy and spares protein; it may be of value in combating acidosis (particularly if a kind susceptible to the special action of glucose is present), and, if given in hypertonic solution, it has been said to bring about the rapid absorption of parenterally administered fluid (that is, there is an internal transfusion

15. At present we do not believe that 20 per cent glucose solution should be used. Tisdall, F. F.; Drake, T. G. H., and Brown, A.: Studies on the Carbohydrate Metabolism in Infants, J. Lab. & Clin. Med. **10**:1 (June) 1925; The Carbohydrate Metabolism of the Normal Infant, Am. J. Dis. Child. **30**:675 (Nov.) 1925. Talbot, F. B.: The Use of Glucose in the Treatment of Disease in Children, Boston M. & S. J. **192**:1000 (May 21) 1925.

of fluids from the tissues into the blood) and to promote diuresis. We believe, however, that there is no special indication for the use of a glucose solution in this malady save that of energy supply; its usefulness in other respects is adequately met by other procedures as described in this paper. If it is desired to give glucose because of its food value, the sugar can be given by mouth in a 2 to 5 per cent solution, subcutaneously in a 5 to 10 per cent solution or intravenously in a 10 per cent solution.[16]

It should be stated, however, that if glucose solutions are of demonstrated special value in the treatment of alimentary intoxication, they should be employed whether or not their use is theoretically indicated. We are still open-minded on the subject; it may be that the beneficial effects of transfusions, so much used by us, are so great that they overshadow the lesser special good which may be derived from the parenteral injection of glucose solutions.

In our opinion, the distention which follows the administration of a glucose solution into the peritoneal cavity prohibits, except in rare instances, its use in that manner.

By mouth, as already stated, we give water; we have tried Ringer's solution and 2 to 5 per cent glucose both in water and in Ringer's solution. We have been unable to observe, as yet, any advantage in any solution over water.

In a few children with marked slowing and enfeeblement of the heart, we have used, at the suggestion of Dr. J. M. Mitchell, a continuous drip clysis of Ringer's solution containing enough epinephrine to make a 1:200,000 concentration. Whether this procedure is of special value can be ascertained with difficulty; in any case, I know of no cardiac stimulant other than epinephrine which can be of value to these patients.

TRANSFUSIONS OF BLOOD

After the administration of fluids, patients with intestinal intoxication often show astonishing improvements within a period of less than two hours. This improvement is often temporary and misleading. It seldom persists in severe cases, even when adequate fluid intake is maintained. It is for this reason that the administration of fluid should be

16. I am informed by Dr. F. F. Tisdall, of the Hospital for Sick Children, Toronto, that glucose can be administered with beneficial results to infants with intoxication according to the following program: (*a*) Intravenously, 15 cc. per pound of a 10 per cent solution, twice daily. The amount of glucose lost in the urine is negligible even when the solution is given rapidly; (*b*) subcutaneously, 10 to 15 cc. per pound of a 10 per cent solution, thrice daily; (*c*) orally, as large amounts as possible of a 5 per cent solution; more concentrated solutions are likely to produce vomiting. It is obvious that the energy supplied to the body from glucose administered according to this program is very considerable. Tisdall, Drake and Brown believe that the promotion of glycogen formation by glucose is important in intoxication because "it is known that the presence of glycogen helps protect the organism against toxemia."

reinforced by a blood transfusion in practically all cases, regardless of an apparent initial improvement. I have the impression that it is best to give parenteral fluid first and wait at least one hour thereafter before giving blood intravenously. There seems to be less shock to the patient when this procedure is followed than when transfusion is performed at once. The amount of blood which may be given to infants with intoxication, with beneficial results, is amazing. Our transfusions have varied in amounts from 20 cc. of blood per kilogram of body weight to 60 cc.; few children receive less than a total of 75 cc. of blood and few more than 200 cc. The amount of blood given is proportional to the malnutrition and the degree of dehydration; that is, the more marked these are, the greater the quantity of blood given per kilogram of body weight. I am distinctly of the impression that initial transfusions of amounts less than 100 cc. are relatively ineffective.

We have used the citrate method of transfusion entirely. Regardless of the age of the child, we give blood only from donors of the same blood group as the patient, or, rarely, from group 1 (Jansky) donors. We have not seen severe reactions follow transfusions in these cases. It has been our experience that babies in general and those with intoxication in particular, stand transfusions extraordinarily well. We have found that exceptions to this rule are most likely to occur in infants who have a severe secondary anemia and an infection.

We repeat transfusions of blood every twenty-four hours during the course of the first few days if the patient does not seem to be making satisfactory improvement, or does not maintain continuous progress. We have rarely performed transfusion more than three times on any patient with intoxication. As already stated, we have usually found that the first transfusion can be, and, to achieve maximum effectiveness, must be, large, but if blood is given subsequently, the amounts should usually be less with succeeding transfusions, that is, totals of from 75 to 150 cc., depending on the size of the patient. Experience has taught the necessity of being cautious, because some patients do not react well to large transfusions repeated within a few days of each other. Less benefit is expected from repetition of transfusions in the treatment of intestinal intoxication than from the first transfusion.

It is impossible to state with exactness in just what manner transfusion helps these patients; both quantitative and qualitative changes in the blood are quickly brought about so that improvement in function of the circulatory renal and respiratory system—and thus of the cells throughout the organism—is made possible. Marriott applied the methods of investigation developed in the study of surgical shock[5] to intestinal intoxcation, and found that in many respects the pathologic physiology in the two conditions is the same. Experience in the late war

gave abundant proof that in shock the administration of fluids aids in the restoration of blood volume and normal circulatory function, but that in severe cases a transfusion of blood is by far the most effective form of treatment. Similarly, although we do not attribute the good results of our plan of treatment of intestinal intoxication to any single measure, but to the combination of measures, we do feel strongly that blood transfusion is *a* most powerful, if not *the* most powerful weapon at our disposal in the treatment of this condition. We believe that the great importance of transfusion in the treatment of intestinal intoxication is not generally appreciated, and that we are on very safe ground in advocating the widespread use of this important therapeutic measure. It is difficult to say whether or not any patient ill with intoxication will not suddenly, without warning, collapse and die. Also, the brilliant effects of the parenteral administration of fluids may give a false feeling of security. Even in patients on whom transfusions have been performed, unexpected collapse and death may occasionally occur. Unmistakable indications for a transfusion may come too late for that treatment to be any longer effective. Having knowledge of these facts, therefore, we have felt that it is better to err in subjecting the patient to unnecessary transfusion rather than to withhold a treatment which subsequent developments may show might have been a life saving measure. We believe that our general good results in the treatment of this malady are due to the fact that we have found out that we cannot discriminate correctly, and foretell which patients are safe without transfusion.

We have seldom used the intraperitoneal injection [17] of blood in patients with intoxication, because we believe that intravenous treatment is the therapy of election when there is marked concentration of the blood. Indeed, though my experience has been inadequate, I have obtained the impression that the intraperitoneal injection of blood in cases of this kind may be harmful rather than helpful. In a few of our cases, when venapuncture could not be done, citrated blood was given intraperitoneally. No beneficial results seemed to follow and, indeed, the general condition of these infants did not seem to be so satisfactory as before treatment. Furthermore, distention developed and persisted for several hours, so that Ringer's solution could not be given into the peritoneal cavity or satisfactorily into the subcutaneous tissues of the abdominal wall. Possibly the circulatory function is so greatly depressed in these patients that blood in the peritoneal cavity cannot be absorbed at a rate or in an amount which makes the blood of any value in restoring blood volume.

17. Siperstein, D. M., and Sansby, J. M.: Intraperitoneal Transfusion with Citrated Blood. Experimental Study, Am. J. Dis. Child. **25**:107 (Feb.) 1923.

We have had no experience with exsanguination transfusion, as introduced by the late Bruce Robertson[18] of Toronto, and used by Brown and Boyd[19] in the treatment of patients with intestinal intoxication. This procedure finds its justification in the premise that the blood of the patient with intestinal intoxication is of a poor quality (that is, has become so altered as no longer to serve its purpose properly or contains toxins or other substances of an injurious nature), and that the blood of the donor is of good quality and may contain antibodies or other substances which are of benefit to the patient. Hence, the aim in exsanguination transfusion is to effect the greatest possible substitution of the blood of the donor for the blood of the patient. Though the hypothesis at the basis of exsanguination transfusion in one respect or another may be true, there are certain practical considerations which militate against the usefulness of this treatment. The procedure is difficult from the technical standpoint, except for the experienced, and increases the risk of accident to the patient. Moreover, it must be remembered that the abnormal conditions in intestinal intoxication are not in the blood alone, but are also in the tissues. A restoration of the blood to its normal condition in the sense of rendering it free from injurious substances is only one desideratum, and that perhaps of subsidiary nature. A restoration of the blood in a quantitative sense and, to a large extent, also, in a qualitative sense, can be effected by ordinary transfusion.

WATER DIET

The feeding of patients with intoxication is a subject about which there is more disagreement, perhaps, than arises concerning any other therapeutic procedure. Some pediatricians feel that those infants, at least who are malnourished, should be fed throughout the illness. On the other hand, there are followers of Marfan,[20] who has been a consistent advocate of a "water diet." Marfan credits the use of a water diet in the treatment of diarrhea to Luton, who used it in Asiatic cholera. Whatever may be the reasons, it is my opinion also that a period of starvation during the stage of toxemia is desirable in the treatment of intestinal intoxication. The fact that some infants are fed throughout their illness and thrive satisfactorily no more invalidates

18. Robertson, B.; Brown, A., and Simpson, R.: Blood Transfusion in Children, Northwest Med. **20**:233 (Aug.) 1921; Blood Transfusion in Severe Burns in Infants and Young Children, Canad. M. A. J. **11**:744 (Oct.) 1921.

19. Brown, A., and Boyd, G.: Acute Intestinal Intoxication in Infants, Canad. M. A. J. **13**:800 (Nov.) 1923.

20. Marfan, A. B.: Traite de l'allaitement et de l'alimentation des enfants du premier age, Ed. 3, Paris, Masson et Cie, 1920; Les affections des voies digestives dans la premiere enfance, Paris, Masson et Cie, 1923.

the use of a starvation period than does the fact that some infants with intoxication recover without transfusion invalidates the use of that treatment.

Starvation may be openly carried out, or may be somewhat camouflaged by the use of tea, a very thin gruel, or a weak (2 per cent) glucose solution. The duration of the period of starvation advocated by those who employ it is a controversial point. Finkelstein [21] does not give food for a period of six to thirty-six hours. Monrad [22] starves his patients until all symptoms which he regards as toxic have disappeared; in some cases this period lasts for as long as twelve days. Monrad's results are given in table 1.

It is possible that those of Monrad's patients who could not withstand starvation died within the first three days. On the other hand, many of the deaths from intoxication occur within the first few days,

TABLE 1.—*Monrad's Statistics Showing Results Obtained in Treatment of Intestinal Intoxication by Water Diet and Subcutaneous Saline*

Duration of Water Diet	Number of Patients	Recovered	Died	
Up to 3 days (24 hours)	110	87	23	= 21%
4 days	61	56	5	
5 days	46	38	8	
6 days	36	30	6	
7 days	15	11	4	
8 days	11	8	3	= 15%
9 days	7	6	1	
10 days	3	3	0	
11 days	1	1	0	
12 days	1	1	0	

no matter whether the patients are fed or starved. Marfan [20] states, that, if after three days of treatment by a water diet and the subcutaneous infusion of salt solution, the patient shows no improvement, the prognosis is absolutely bad. However, Marfan and Monrad do not use transfusion, by means of which patients are frequently carried beyond the dangerous three day limit laid down by Marfan and recover.

While we believe that theoretically the point at which starvation should be terminated is established by the disappearance of toxic symptoms, in actual practice we have found it inadvisable to adhere strictly to Monrad's precept. There are difficulties to be faced in making emergence from a toxic state the sole criterion for a resumption of feeding; these may be briefly discussed. In the first place, it is impossible to say in many cases just when all toxic symptoms have disappeared. In the second place, another factor, the nutritional state and vigor of the

21. Finkelstein, H.: Lehrbuch der Säuglingskrankheiten, Zweite Auflage, Berlin, J. Springer, 1921.

22. Monrad: Zur Behandlung der akuten toxinfektiösen Gastroenteritis mit besonderer Bezugnahme auf die heilsame Wirkung einer protranierten Wasserdiät, Monatschr. f. Kinderh. **25**:468, 1923.

patient, must be taken into consideration. If the baby is well nourished and has been vigorous, as can be judged by the condition of his body and by the history, he is able to withstand starvation. He may die, or may be so sick as to be close to death, when first seen. But if he dies, it will be as a result of intoxication or infection, not as a result of starvation. Indeed, such a baby, surviving, steadily improves under the influence of starvation and at the end of three or four days on a water diet appears in so vigorous a condition often that one wonders why he ever thought of the possibility that the baby would not withstand starvation. On the other hand, prolonged starvation is to be feared in severely malnourished infants, especially in atrophic babies, that is, in those who have no subcutaneous fat on the face as well as none on the abdomen, trunk and extremities. Such babies have probably lost already one-third or more of their body weight, and are in danger of death as a result of destruction of their structural tissues. Starvation is also to be feared if the baby is not only poorly nourished, but also is very young or premature. As a matter of fact, one is often unable to distinguish between signs and symptoms dependent on malnutrition and feebleness and those dependent on the sickness of the baby.

The period of starvation has varied in our patients from twelve hours as a minimum to 120 hours as a maximum; usually, the period is from twelve to forty-eight hours. In the baby who has a fairly well-nourished body, no matter how sick or how close to death he seems to be, we have no fear of several days of starvation and do not begin feeding the patient until, in our judgment, the stage of toxemia has passed. But the majority of cases are in the group of feeble and atrophic babies, and in these we have not waited for complete emergence from toxic symptoms (although this may have taken place), but have given food after periods of starvation averaging from twelve to forty-eight hours. In behalf of a starvation period, it is only fair to say that malnourished babies seem to withstand starvation much better than would be supposed possible by one who has not practiced this form of therapy. The system used by us to break the fast (that is, the method of gradual daily caloric ascent starting at a very low level) provides a marginal safety zone in treatment—a period when the patient is neither completely starved nor adequately fed. Thus, we hope that, if the patient is well nourished, our error, if any, will be on the side of unnecessarily prolonged starvation; if very young and feeble and if malnourished, on the side of too early resumption of feeding. I have no doubt that if we were gifted with foresight, we might, by omitting or shortening the starvation interval and by rapidly increasing the caloric intake, abbreviate the convalescent period. But, lacking this foresight, it seems wise to stand by a plan of treatment which affords hope of recovery to the largest number of patients.

THE PROCEDURE IN RESUMPTION OF FEEDING: QUANTITY OF FOOD

When feeding is reestablished, it should be done in a very gradual manner, that is, the organism should be required to reassume its former burden by small daily increments. An effort should be made to keep the total daily food intake well below the supposed tolerance of the infant. Usually, the normal caloric requirement of food for any given baby, who has been the subject of intestinal intoxication, should not be reached before a week or ten days have elapsed after the resumption of feeding. I think this policy should be followed, no matter how well a child may appear to be doing. In practice, we have followed Finkelstein's [21] method of increasing in a staircase manner the quantity of food; the food is given in small amounts at frequent intervals. We have found this method far more satisfactory than our former unsystematic manner (chart 5) of varying the food each day according to a new guess at the patient's tolerance, a haphazard method which constantly led to disastrous mistakes of overfeeding; costly retreats were often forced thereby. On the first day, the infant receives from 10 to 20 calories per kilogram of body weight, and each day the caloric intake is increased by from 5 to 15 calories per kilogram. If the child does very well at the end of three days, the increment may be made larger. In terms of total calories, the child is started out on an intake of about 50 calories daily, and the increase is at first 25 calories daily and later 25 to 50 calories. In terms of volume and interval, on the first day the patient is usually given ten feedings of 10 cc. each, the feedings being given at two-hour intervals. The daily increment at first is from 5 to 10 cc. per feeding; at the end of three or four days, if the child is doing well, the increments are made larger and the interval lengthened.

It should be emphasized that throughout the period of starvation and inadequate food intake, fluid must be administered parenterally and by mouth, according to the condition of the patient with respect to dehydration.

The weight curve of patients treated in the manner outlined in this paper does not show wide fluctuations. The curve is kept fairly stable at first by the parenterally and orally administered fluid; as the amount of such fluid required diminishes, the amount of food which should be administered increases. In the average case, on about the fifth or sixth day, little, if any, parenteral fluid is required and the caloric intake is about 50 or 60 calories per kilogram per day. After this point has been attained, as shown by a level or rising weight curve, we usually proceed for the succeeding week or ten days without increase in the diet more frequently than every second or third day. The caloric increments are small. This rule is not invariably followed, but in general is safe. If the child is vigorous and bids fair to make a rapid recovery, one can

advance quickly to the caloric intake required for growth. Even on a basal diet, these patients, particularly those who are fairly well nourished, often make considerable gains in weight for a week or ten days. This is a recovery or reparative period when the weight lost during the illness, due to the inability of the tissues to retain water, is regained. Thus the gain in weight is due largely to retention of water.

We have been led to adopt the conservative course outlined in the foregoing, because of the fact that patients who have had intestinal intoxication are prone to recrudescences, from which recovery is less likely than from the initial attack. Treatment of recrudescences and recurrences are often not satisfactory.

THE KIND OF FOOD

In regard to the kind of food to be given in cases of intestinal intoxication, I am under the impression that the matter has received undue emphasis considering the paucity of facts. There is little agreement among pediatricians on this subject; what one clinician regards as nectar is regarded by others as poison. I have seen various milk mixtures used, namely, breast milk, protein milk, protein milk with sugar, dairy buttermilk, skimmed lactic milk,[23] alone and with added carbohydrate, either sugar or starch, or both, boiled sweet skimmed milk,[24] boiled sweet whole milk diluted with water and with added sugar. Skimmed breast milk is advocated in some German clinics and a vegetable soup in others, as well as in certain French clinics. Some physicians prefer to use whey in these cases; others a thin or thick gruel. From my own experience, I can only say that the character of the food has not seemed a matter which plays a leading part in the successful treatment of intestinal intoxication. In the early stages, at least, I have observed satisfactory results with thin gruels. Any cow's milk mixture seems as satisfactory as any other, provided that it is cooked, does not contain over 20 or 30 per cent of the total calories in fat and has a concentration of little less than that of breast milk. In protein milk, 55 per cent of the total calories are given in fat, but the fat is apparently well tolerated. I do not believe, however, that protein milk is the most satisfactory food for these patients. I have had more experience with dried skimmed milk in which 2 to 5 per cent dextrimaltose, barley or rice flour has beeen cooked, and the mixture subsequently fermented by lactic acid bacilli or soured with lactic acid, than with any other food except protein milk. This food is usually supplanted in a week by a

23. Sometimes the milk was fermented by lactic acid bacilli, and sometimes soured by lactic acid.

24. I have had no experience with raw milk, sweet or sour (except protein milk), in the treatment of intestinal intoxication.

more concentrated mixture, such as boiled whole milk with added sugar and cereal; the mixture may or may not be soured; water may be added but only for the purpose of supplying food to the patient. I cannot state that I have observed anything which convinces me beyond doubt that sour milk mixtures have outstanding virtues in the treatment of this condition; I prefer, as a rule, to use lactic milk mixtures because of the widespread belief in their superiority over sweet milk mixtures in the feeding of most sick infants. Also, because I am aware of no evidence which would indicate that the acidity or other qualities peculiar to sour milk are in any way harmful. I have no definite impression as to the merits of breast milk in this malady other than a feeling that in very young, feeble babies this food should be tried in preference to any other.

It may be that differences in the quality of the food, other than those which I have mentioned, are of great importance in the treatment of intestinal intoxication, but I have failed to perceive what these important differences are. When I have thought that this or that mixture was essential for the particular type of case under discussion, I have usually discovered that I was influenced by prejudice rather than by accurate observation. The fact that so many mixtures are recommended for the same disease is competent testimony that either they are all fundamentally the same, or else, if different, their respective virtues are not in any sense outstanding. It seems to me that there are so many conflicting opinions on this point because food is given to many patients with intoxication before they are in a condition satisfactorily to utilize it; then the results, whether recoveries or deaths, are ascribed to some particular quality of the diet rather than to the food as food and to other exceedingly important factors.

THE USE OF DRUGS

Acidosis[11] of severe degree is present in a considerable number of patients with intestinal intoxication. Whatever be the nature of the acidosis, it is likely that its development is dependent in large measure on increased blood concentration and the attendant blood, circulatory, respiratory and renal disturbances. It has been our experience, together with that of many other observers, that the intravenous administration of a solution of sodium bicarbonate causes the symptoms of acidosis to disappear, at least temporarily, but the patient does not improve. On the other hand, if treatment is focused on a restoration of the blood volume, not only do the symptoms of acidosis disappear (although more slowly than with intravenous bicarbonate), but in most instances the patient shows other evidences of improvement. We do not, therefore, use intravenous injections of bicarbonate of soda. I believe, however, that it is often advisable to give, at the onset, to those patients who

clinically or by laboratory tests show unmistakable evidences of severe acidosis, one or two doses of soda of 3 to 6 Gm. each in 60 to 90 cc. of ice-cold water. The soda is given through a stomach tube after gastric lavage. This lavage is not carried out until at least one hour has elapsed after the intraperitoneal or subcutaneous injection of Ringer's solution; if the soda is given earlier, it is almost certainly vomited. The second and third doses of soda may be given at three hour intervals; I believe it is never wise to give more than two, or, at most, three doses. The use of alkalis in the manner indicated is, I believe, beneficial and does not give rise to the danger of alkalosis which may occur with the indiscriminate use of soda.

On occasion, sedatives for the very restless, hyperirritable baby are indicated. Indeed, it seems to me very important that if a patient with intoxication continues awake and restless after the administration of parenteral fluid and the transfusion of blood, he should be given a sedative and freed from all annoyances for a period of about six hours. Morphine sulphate hypodermically is probably the best sedative to use.

It seems reasonable that benefit might be had from catharsis for certain patients who are seen at or near the onset of their sickness, and presumably have a considerable food residue in their gastro-intestinal tract. This food residue is doubtless the source of, or culture medium for, the production of toxic products,[25] or acts as an irritating foreign body on an alimentary tract which is losing or has lost its ability to function effectively. Aid in the removal of this "foreign body" at the opportune moment might conceivably shorten the course of the illness. There seems to be no justification in theory or practice for the use of cathartics after the watery diarrhea has set in.

I have observed no benefit from the administration of camphorated tincture of opium with the idea of lessening the number of stools. The sedative value of the drug may, of course, be of value in certain cases.

TREATMENT WHEN PATIENTS ARE REFRACTORY OR HAVE RECURRENCES

There are, of course, patients with intestinal intoxication who do not respond to the treatment advocated in this paper (chart 4); there are others who, when they are apparently convalescing satisfactorily, have recrudescences of the toxic symptoms. Such misfortunes are most likely to occur in patients who have an infection and in those who are markedly malnourished. Any patient, also, whose caloric intake during convalescence has been, apparently, too vigorously pressed, is prone to have his toxic symptoms return. As already pointed out, recurrences are

25. Mellanby, E.: An Experimental Investigation on Diarrhea and Vomiting of Children, Quart. J. Med. **9**:165 (April) 1916.

more difficult to treat successfully than was the initial illness. With each "break," the ability to come "back" seems to diminish.

Outstanding in number and in difficulty in the group of patients under immediate consideration are those who have infections. The most difficult problem in infant feeding, practically untouched in any effective manner, is, I believe, the atrophied infant with infection. It may fairly be questioned whether the problem here does not lie more in the field of bacteriology and immunology than in that of infant nutrition.

In treating the infant who does not respond, or in whom symptoms of intoxication recur, it is very difficult to know what to do and impossible to lay down rules-of-thumb. The best mode of procedure is by no means clear in my own mind. So far as I know, one should adhere as closely as is permitted to the principles discussed in this paper, but should be prepared to make such modifications of the various procedures as the special symptoms and reactions of the individual patient seem to demand. Without doubt, fluids must be adequately supplied and transfusions judiciously used. The latter may be given two or three times a week. Such measures, according to our present knowledge, must be regarded as constituting "supporting" treatment, calculated to enable the patient to "carry on" until in time the necessary adjustments of a metabolic, immunologic or other nature are made. No therapeutic or dietary measure with which I am familiar approximates in value the transfusion of blood to these patients.

I cannot speak with such definiteness, however, in regard to the feeding of the infants in this special group. Torn between a desire to withhold food because of toxic symptoms and a compelling belief that food must be given because of the severity of the malnutrition and the feebleness of the child, I am sure that, to a large extent, one simply "muddles along." But one must adopt some policy and, probably, in most instances, we do not pursue quite a middle course but incline to run the risk of overfeeding rather than underfeeding, relying on giving concentrated food in small amounts at frequent intervals. The period of water diet may be repeated, as seems indicated, once or, possibly, in rare instances, twice, but the duration is never long, from eight to twenty hours. The caloric intake after the period of starvation is usually advanced rapidly, sometimes abruptly, to the basal requirement or above it. If all seems to go well, an increase in the caloric intake may be made every second or third day; but it is usually only after these patients are well along the road to convalescence that we consider giving the large amount of food required to meet their total requirements. As a matter of fact, these infants have very poor appetites, as a rule, and at this stage are usually receiving about all the food we can get them to take.

When these patients do badly, it is often difficult to point out just where the difficulty lies. The troublesome symptoms which arise are not the same in all cases. In some infants, vomiting is the chief difficulty encountered; in others, refusal of food; a combination of these two symptoms presents a formidable problem. Some infants have almost continuous distention; this is an ominous sign.

The reactions of patients to identical treatment for the same symptoms are by no means uniform. In the majority of patients in this group, we have been obliged to try one procedure after another. It is not advisable to continue using starvation periods, when that form of treatment has been tried and found valueless for the particular patient. One can try lavage and gavage, tube feeding without lavage, small amounts of concentrated food at hourly or two hourly intervals, nasal drip feeding, ice-cold food, fat-free milk mixtures, milk mixtures thickened with cereal, sour-milk mixtures, 5 per cent glucoes solution, broth enriched with carbohydrate. One never knows beforehand what food or method of feeding is most likely to be successful, and sometimes none is. The diarrhea which, in greater or less severity, is a pretty constant symptom, must be disregarded so far as special treatment is concerned.

The infection from which an infant with intestinal intoxication is suffering may, of course, be amenable to special treatment; e. g., otitis media, mastoiditis, furunculosis. Surgical measures are certainly to be employed in many cases. But usually, perhaps, the infection is dealt with most successfully just as is the intoxication, that is, by keeping the fluid intake adequate and by transfusions of blood. The possible presence of antibodies in the donor's blood must be recognized as important in this connection. Marriott [26] and Floyd [27] have recently emphasized the rôle of streptococcus infections of the mastoids in certain infants with intestinal intoxication.

They believe that simple drainage offers hope of cure in these patients. It may be pointed out that a streptococcus infection of the mastoids can probably be related etiologically to only a limited number of these cases. An infection with the streptococcus would not seem to account for the fact that intestinal intoxication is most frequently seen in hot weather, that it takes place in infants in whom no evidence of any infection of the upper respiratory tract is found, and that it may occur with a variety of infections, not all of which are due to the streptococcus. Since the most common serious infections to which infants are susceptible are those of the upper respiratory tract and of the middle ear, and

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26. Marriott, W. M.: Further Observations Concerning the Nature of Nutritional Disturbances, Tr. Am. Pediat. Soc. **37**:38, 1925.

27. Floyd, M. L.: Masked Mastoiditis Simulating "Alimentary Intoxication," (Anhydremia), Arch. Otolaryng. **1**:411 (April) 1925.

since the streptococcus is perhaps the most frequent infecting bacterium when these infections are severe (and is sometimes demonstrable in the blood stream as well as locally), it naturally follows that a large number of infants develop intoxication when suffering from infection with this particular organism. We have seen intoxication in infants with bronchopneumonia, pyelitis, dysentery and furunculosis; also, typical cholera infantum in measles and in staphylococcus as well as in streptococcus septicemia.

EFFECTIVENESS OF TREATMENT

It is my impression that the mortality from intestinal intoxication, treated, as formerly, by enteral and parenteral fluid, intravenous injections of a bicarbonate of sodium solution and milk mixtures, supposed to be more or less specific for diarrhea, is about 80 or 90 per cent. Holt and Howland [28] state that: "True cholera infantum is nearly always fatal." According to Morse and Talbot,[29] "It is very seldom that a baby recovers from this disease. Death usually takes place during the

TABLE 2.—*Statistics of Patients with Intestinal Intoxication in New Haven Hospital, 1922-1925 (Inclusive)*

	Number of Patients	Recovered	Died	Per Cent Died
Advocated treatment carried out	36	24	12	33
Advocated treatment not carried out	19	5	14	70
Patients admitted in extremis and died in less than 12 hours after admission; also, patients who were taken home against advice	9	..	9	..
Total	64			

first forty-eight hours after the onset." Similar statements are found in other textbooks. With a small hospital service, it is impossible in a short time to accumulate an imposing array of statistics to show the effectiveness of the treatment which has been outlined. Statistics do not absolutely settle a matter of this kind unless a large number of similar cases are differently treated and results are compared. However, it can be said with certainty, I believe, that with the plan of procedure here advocated, a goodly majority of infants with intoxication recover. I have gone over the histories of all infants with acute gastro-intestinal disturbances in this clinic during the past four years, and have selected only the ones in which the diagnosis of intestinal intoxication seemed justified beyond doubt. There were sixty-four such patients, and the facts in regard to the termination of the cases are summarized in table 2.

28. Holt, L. E., and Howland, J.: Diseases of Infancy and Childhood, Ed. 8, New York, D. Appleton & Company, 1922.

29. Morse, J. L., and Talbot, F. B.: Diseases of Nutrition and Infant Feeding, Ed. 2, New York, The MacMillan Company, 1920.

Some of the patients were so ill that it seemed probable they would die before they could be transferred from the admitting room to the ward.

It will be seen from the table that the mortality for cases of intestinal intoxication in which treatment followed no comprehensive plan, but was guided by symptoms as they arose, is 70 per cent. All of the patients in this group received parenteral fluids; some were transfused; some were starved for short periods; practically all, when feeding was begun, received at least 50 calories per kilogram; but none of them received the benefit of the comprehensively planned treatment advocated in this paper (chart 5). In looking over histories of the patients in this group, and viewing the treatment throughout the illness in retrospect, one is astonished to find that many procedures seemed illogical and without guidance of underlying principles. Often there was a series of apparently meaningless variations and inconsistencies—large quantities of water given one day and very little the next, a feeding or two omitted here and there, a high caloric intake during one period and low during another, a dose of soda now and then, a transfusion on the third or fourth day, etc.

In contrast is a mortality of 33 per cent for these patients treated in fair accord with the principles advocated in this paper. From this time forward, I believe that, with the same type of patients as in the past and with the principles of treatment as discussed in this paper faithfully adhered to, our mortality will not exceed 25 per cent.

A consideration of the duration of the illness is an important factor in prognosis; the longer a patient has been in a state of intoxication, the less favorable is the outlook. The severity of symptoms and the degree of dehydration and acidosis are, however, of relatively little value in prognosis. Those patients in our series who were treated according to the advocated procedure, and who constitute an exception to the rule of majority recovery, are, for the most part, the ones who had both severe infection and marked malnutrition as well as intoxication; one views such cases without confidence of a favorable outcome.

In addition to the malnourished babies with infections, other patients whose deaths have raised our mortality rate were those whose condition on admission were deceptive; these patients took the physician off his guard. On more than one occasion the seriousness of an infant's condition was misjudged, and a short cut in treatment and to convalescence was attempted, usually, by omitting transfusion and by reducing the period of water diet and restricted food intake. The results in several of these cases were unexpected fatalities, which served as warnings that in treating this condition all the prescribed measures should be employed from the outset.

It is needless to discuss the patient who is admitted in a moribund state and dies within a few hours. Such patients, however, are started on treatment and, sometimes, to the astonishment of everyone seeing them, have responded satisfactorily.

SUMMARY AND CONCLUSIONS

A comprehensive plan of treatment for routine use in cases of intestinal intoxication has been outlined and discussed. This plan is the result of a gradual evolutionary development based on clinical experience. It is not my desire to give the impression that the treatment advocated is the only one which may be employed in intoxication. But, from experience and from discussions with colleagues in various clinics, we have come to believe that the procedures outlined constitute in principle the treatment which will be attended most frequently with success. And, while success, in my opinion, is made possible by adherence to the principles on which the treatment is based, we do not advocate a rigid, narrow attitude in applying them in the care of the individual baby. All patients with intestinal intoxication are seriously ill and, in this clinic, are treated from the *outset* on the basis of that fact. Distinctions in regard to clinical types are not made, and laboratory findings are not used as the chief guides in determining treatment. I realize, of course, the great importance of laboratory investigations in intestinal intoxication and am as fully conscious as anyone that all true progress in developing a specific therapy must come as a result of the accumulation from the laboratory of one new fact after another. Until the laboratory data are fairly complete and their significance known, however, the therapeutist cannot safely deduce in a strictly rational manner his procedures from facts which are but isolated portions of the whole truth. For the present, I believe that the wise and safe course to follow in treating infants with intoxication is to remove from our minds the conception of correcting specific metabolic disurbances by specific treatment, and to go forward with singleness of purpose to give each patient from the outset the benefit of all therapeutic measures whose effect is to help restore normal function to the cells of the whole organism. This course should be followed, regardless of any evidence from the laboratory as to the normal nature of certain metabolic processes and the disturbed condition of others.

The successive steps in carrying out the plan of treatment advocated conform ideally to the following schedule:

1. Ringer's solution is given intraperitoneally or subcutaneously, or, usually, in both ways. As quickly as possible, blood is taken from the baby and from relatives or friends in order that the blood groups may be determined. Venapuncture is performed on the patient, and blood is withdrawn for culture and chemical studies.

2. A blood transfusion by the citrate method is done; the amount of blood given varies from 20 to 60 cc. per kilogram of body weight; transfusions seldom total less than 100 cc. or more than 200 cc.

3. If the patient has acidosis, the stomach is lavaged, and from 3 to 6 Gm. of bicarbonate of soda dissolved in 40 to 60 cc. of ice-cold water are left in the stomach. This treatment may be repeated once or, possibly, twice according to indications, at three hour intervals.

4. Water is given by mouth, either in fixed amounts at definite intervals, or continuously by the drip method through a nasal catheter.

5. Ringer's solution is administered parenterally as often as there is indication.

6. Transfusion may be repeated once or twice at twenty-four hour intervals if the child does not improve.

7. The patient is given no food by mouth, until toxic symptoms have disappeared or greatly diminished. When food is given, the amount is very small and the interval is two hours; the caloric value is raised daily by definite small increments. On the first day a total of about 50 calories is given, on the second 75, on the third 100, etc.; if all goes well, the increments may then be made larger and the total caloric requirement attained in a week or ten days.

8. Modification of the procedures as regard feeding is often made when the patient is an atrophic baby with severe infection.

PROGRESS IN PEDIATRICS

REVIEW OF THE LITERATURE ON SYPHILIS*

(Continued from page 116)

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THE TREATMENT OF SYPHILIS

Since the last review of syphilis in this journal, several new antisyphilitic remedies have been brought forward and several that have had some previous use have attained greater prominence. Among the new preparations sulpharsphenamine and flumerin seem of definite merit. Bismuth, which was suggested for use in treatment many years ago, has had its usefulness established during the past few years. Tryparsamide has been extensively employed in cases of neurosyphilis. Perhaps of greater importance than these additions to our means of treatment of syphilis is the fact, only recently generally recognized, that in sodium thiosulphate, a drug relatively harmless, we have an excellent remedy for many of the ill effects which may be produced by the antisyphilitic drugs.

SULPHARSPHENAMINE

Voegtlin, Johnson and Dyer,[45] late in 1922, reported the preparation of a new arsenical, namely, sulpharsphenamine, which has some definite advantages over the older arsphenamines in common use. Sulpharsphenamine is quite stable, requires no elaborate technic for administration and may be administered intramuscularly, with only little disturbance to the patient. Certain other advantages are claimed for it by some authors. This drug has not received universal approval, as certain unpleasant and even serious by-effects, such as arsenic dermatitis, are reputed to be more frequent with sulpharsphenamine than with the other arsphenamines.

In white rats the minimum lethal dose of sulpharsphenamine is between 320 and 480 mg. per kilogram. No toxic symptoms are produced by two thirds of this dose. The maximum toxic effect was manifest within twenty-four hours of the administration. Standing at room temperature twenty-four hours did not increase the toxicity of a solution of sulpharsphenamine. Thus, sulpharsphenamine is much less toxic and more stable than arsphenamine or neo-arsphenamine.

The trypanocidal power, as tested in rats infected with *Trypanosoma equiperdum,* was equal to that of neo-arsphenamine, though the maxi-

45. Voegtlin, C.; Johnson, J. M., and Dyer, Helen: Sulpharsphenamine: Its Manufacture and Its Chemical and Chemotherapeutic Properties, Pub. Health Rep. **37**:2783 (Nov. 10) 1922.

mum effect was observed from two to three days after treatment, whereas with neo-arsphenamine the maximum effect is manifest in twenty-four hours. The effect was more rapid with intramuscular than with intravenous administration.

The spirocheticidal power, as tested in rabbits infected with *Spirocheta pallida,* indicated that 15 mg. of sulpharsphenamine equals 15 mg. of arsphenamine in value, although the percentage of arsenic in the two preparations is 21 and 30, respectively. The spirochetes had disappeared from the lesions twenty-four hours after treatment.

In the treatment of syphilis, sulpharsphenamine is as well tolerated intravenously as the other arsphenamines, but when employed intramuscularly it is much superior because of the lesser amount of pain. For intramuscular use, solutions containing from 30 to 40 per cent of sulpharsphenamine are less irritating than those more diluted. The chief points of advantage claimed for sulpharsphenamine over other arsphenamines are (1) that it is easier to manufacture; (2) it has greater stability; (3) it has greater constancy of action, and (4) it is more suitable for intramuscular and subcutaneous injection.

Boone and Weech [46] used sulpharsphenamine in the treatment of twenty-one infants under 1 year of age, giving 20 mg. per kilogram weekly for six weeks, with a repetition of the course after two months rest. The Wassermann reaction became negative after the first course of treatment in 55 per cent of the cases. It is concluded that infants will tolerate 1.47 times as much arsenic in the form of sulpharsphenamine as they will in the form of neo-arsphenamine.

Doble [47] prefers sulpharsphenamine to the older preparations in the treatment of adults. He is of the opinion that any arsenical is more effective when given intramuscularly, and that sulpharsphenamine is as efficient as neo-arsphenamine in the treatment of syphilis at any stage. Administered intramuscularly, sulpharsphenamine causes only a little inconvenience, and does not require dietary preparation of the patient. It is particularly useful in patients whose veins are not accessible.

Irgang [48] finds that sulpharsphenamine compares quite favorably with neo-arsphenamine in the treatment of secondary syphilis, and believes that the subcutaneous administration is less effective than intramuscular.

Raiziss, Severac and Moetsch [49] found the chemotherapeutic index

46. Boone, F. H., and Weech, A. A.: The Treatment of Early Hereditary Syphilis with Intramuscular Injections of Sulpharsphenamine, Am. J. Dis. Child. **27**:39 (Jan.) 1924.

47. Doble, F. C.: Sulpharsenol in Syphilis and in Complications of Gonorrhea, Lancet **1**:70 (Jan. 13) 1923.

48. Irgang, S.: Sulpharsenol in the Treatment of Syphilis. A Preliminary Report, Am. J. Syph. **7**:318 (April) 1923.

49. Raiziss, W. G.; Severac, M., and Moetsch, J.: The Chemotherapy of Sulpharsphenamine Toxicity and Trypanocidal Efficiency, J. A. M. A. **83**:1734 (Nov. 29) 1924.

of sulpharsphenamine to be markedly less than that of either arsphenamine or neo-arsphenamine. The trypanocidal efficiency is the same whether sulpharsphenamine is administered by vein or into a muscle.

Halloran [50] used sulpharsphenamine in the treatment of advanced neurosyphilis in thirteen cases. The response was comparable to that seen in similar cases with the use of other arsphenamines, and evidence is presented that sulpharsphenamine penetrated the nervous system better than neo-arsphenamine. In many cases, albumin and casts were found after the seventh or eighth treatment.

In the treatment of 126 cases of various types of syphilis, Stokes and Behn [51] obtained gratifying results with sulpharsphenamine. The Wassermann reaction readily became negative in those subjects recently infected, the results being as good as those obtained with arsphenamine and better than those with neo-arsphenamine. In cardiovascular cases, in which the reaction to the older arsenicals usually is poor, the response to sulpharsphenamine was quite favorable. More cutaneous reactions were observed with sulpharsphenamine than with arsphenamine or neo-arsphenamine.

Belding [52] found the therapeutic effects of sulpharsphenamine to compare favorably with those of neo-arsphenamine, but that it is more toxic. Of the cases in which the sulpharsphenamine was given intravenously, 16 per cent developed dermatitis, and 56 per cent developed varying degrees of neuritis. No such accidents followed intramuscular injection. He advocates a dose of not over 0.7 gm. a week for the average man. In a later [53] publication, he places much less emphasis on the toxic effects. He found the Wassermann reaction to be as favorably affected by sulpharsphenamine as by arsphenamine in both hereditary and acquired syphilis. The Wassermann reaction was affected more favorably by intravenous than by intramuscular injection. He gave sulpharsphenamine in amounts of 1.7 to 2 times the usual dose of neo-arsphenamine, with the development of toxic effects in only one case. Using a titration method for the Wassermann test, he noted that in no instance did a Wassermann reaction of over 16 units become negative as a result of treatment.

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50. Halloran, R. D.: Treatment of Neurosyphilis with Sulpharsphenamin; A Report of Thirteen Cases, Boston M. & S. J. **190**:55 (Jan. 10) 1924.

51. Stokes, J. H., and Behn, C. W.: Serological and Clinical Results in Various Types of Syphilis with Sulpharsphenamin Administered Intramuscularly, J. A. M. A. **83**:242 (July 26) 1924.

52. Belding, D. L.: The Wassermann Test: VII. Sulpharsphenamin in the Treatment of Syphilis, Arch. Dermat & Syph. **9**:470 (April) 1924.

53. Belding, D. L.: The Wassermann Test: XIV. The Effect of Sulpharsphenamin on the Wassermann Reaction, Arch. Dermat. & Syph. **11**:736 (June) 1925.

Fordyce, Rosen and Myers,[54] through animal experiments, concluded that sulpharsphenamine is "2.5 times less efficient" than neo-arsphenamine, and that there is a material danger of its causing purpura if it is not used with care. Sulpharsphenamine gave them no better results than neo-arsphenamine, and showed no special affinity for the nervous system, as has been claimed by others.

O'Leary and Connor[55] have noted two instances in which hemorrhagic purpura followed the use of sulpharsphenamine. They are of the opinion that this event occurs less frequently after sulpharsphenamine than after neo-arsphenamine. Purpura may follow either the intravenous or the intramuscular administration.

TRYPARSAMIDE

Tryparsamide has been employed in all stages of syphilis, but has found its greatest usefulness in neurosyphilis. Moore, Robinson and Keidel[56] found it detrimental in early neurosyphilis, but recommend it in late neurosyphilis, in which the clinical results with tryparsamide were quite gratifying and often remarkable. The Wassermann reaction of the blood was seldom favorably affected, and occasionally the reaction became positive in cases in which it had been negative. Unfavorable sequellae of tryparsamide administration were noted with considerable frequency. Amblyopia developed in ten cases (10 per cent). In four of these the damage was permanent, and in three of the four it was extensive.

In a later publication, Woods and Moore[57] reviewed 240 cases, in which 3,000 tryparsamide treatments had been given. In this group, unfavorable symptoms developed in 17.8 per cent. The chief subjective symptom was a sensation of a dazzling light, as from the sun on bright snow. This occurred in 10.7 per cent of all cases. The chief objective finding was a narrowing of the visual fields, which in some subjects proceeded to complete blindness. The onset usually was gradual, but occasionally was abrupt. These reactions were considered to be due to the drug rather than to neurosyphilis, since nonsyphilitic subjects reacted in the same manner.

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54. Fordyce, J. A.; Rosen, I., and Myers, C. N.: Quantitative Studies in Syphilis from Clinical and Biological Point of View; Localization and Fate of Sulpharsphenamin in Viscera and Its Penetration into Central Nervous System After Intravenous Administration in Rats, Am. J. Syph. **9**:18 (Jan.) 1925.

55. O'Leary, P. A., and Connor, H. M.: Acute Purpura Hemorrhagica as Complication in Treatment of Syphilis, Am. J. Syph. **9**:262 (April) 1925.

56. Moore, J. E.; Robinson, H. M., and Keidel, A.: Tryparsamide in the Treatment of Syphilis, J. A. M. A. **82**:528 (Feb. 16) 1924.

57. Woods, Allen C., and Moore, J. E.: Visual Disturbances Produced by Tryparsamide Treatment, J. A. M. A. **82**:2105 (June 28) 1924.

Lillie [58] states that eye complications are as frequent and as severe with any other arsenical as with tryparsamide.

Ebaugh and Dickson [59] believe tryparsamide to be the best drug yet devised for the treatment of neurosyphilis. In the course of one year's experience, they have been able to return 30 per cent of their paretic patients to their usual work. As untoward symptoms they encountered jaundice, dermatitis, visual disturbances and neurorelapses.

Wile and Wieder [60] found little or no parallelism between the laboratory findings and the clinical course in subjects undergoing treatment with tryparsamide. They found that the cytology and organic solids of the cerebrospinal fluid may or may not become normal, that the Wassermann reaction may not be affected appreciably, but that noticeable clinical improvement occurred in 30 per cent of the cases. Seven paretic patients who had been institutionalized were able to return to their work as a result of treatment. In these investigators' hands, tryparsamide produced no severe untoward effects.

Moore, Robinson and Lyman [61] state that tryparsamide is not to be considered as a substitute for the other arsenicals. The best results were obtained when tryparsamide was used following or in conjunction with arsphenamine. Their dosage of tryparsamide for adults was 3 Gm. weekly for a period of from eight to sixteen weeks. A rest period of from two to four months then followed.

Solomon and Viets [62] have been rather unfavorably impressed with tryparsamide after its use in 100 subjects. The cell count and the globulin content of the cerebrospinal fluid were reduced, but never to normal levels. The Wassermann reaction of the blood was occasionally reduced, but it generally remained unchanged. Five per cent of the patients who had vigorous arsphenamine treatment responded quickly when given tryparsamide. Patients who were making fair progress with arsphenamine treatment were not benefited by a change to tryparsamide. Many of the tabetic patients showed improvement, but not as rapidly as did those receiving intraspinal treatment. Patients with general paralysis

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58. Lillie, Walter I.: Tryparsamide Treatment of Syphilis of the Central Nervous System, J. A. M. A. **83**:809 (Sept. 13) 1924.

59. Ebaugh, F. G., and Dickson, R. W.: The Use of Tryparsamide in the Treatment of General Paralysis. Results of First Year's Experience, J. A. M. A. **83**:803 (Sept. 13) 1924.

60. Wile, Udo J., and Wieder, L. M.: Tryparsamide in the Treatment of Neurosyphilis. Further Observations, J. A. M. A. **84**:1710 (June 6) 1925.

61. Moore, J. E.; Robinson, H. M., and Lyman, R. S.: The Results of Tryparsamide Therapy in Syphilis, J. A. M. A. **83**:888 (Sept. 20) 1924.

62. Solomon, H. C., and Viets, H. R.: A Comparison of Tryparsamide and Other Drugs in the Treatment of Neurosyphilis, J. A. M. A. **83**:891 (Sept. 20) 1924.

manifested no striking improvement with tryparsamide therapy, and many of them did badly. The results were no better than those with arsphenamine, but because of its ease of administration tryparsamide is recommended in selected cases.

Wile and Keim,[63] in a study of 1,000 cerebrospinal fluids, found only little parallelism between the laboratory and clinical results. In only one third of the patients with general paralysis was there a decrease in pleocytosis after eighteen months of treatment. Tabetic subjects showed only little laboratory improvement, although clinical improvement often was marked. In acute cerebrospinal syphilis, the laboratory and clinical findings were most nearly parallel. The finding least influenced was the Wassermann reaction of the cerebrospinal fluid.

The reported cases of hereditary syphilis treated with tryparsamide are few. Stokes and Wilhelm,[64] in a group of 152 patients with neurosyphilis, report six in whom the syphilis was hereditary. Of these, juvenile paresis was diagnosed in five. Tryparsamide treatment gave a good result in one patient and fair results in four patients, while only one subject remained unimproved. These investigators considered tryparsamide to be the last resort rather than the treatment of choice.

Other reports than those cited record observations similar to those already mentioned. Tryparsamide is generally recognized as being of value in the treatment of neurosyphilis. The desirability of watching closely the visual fields is mentioned by most writers.

BISMUTH

According to Grund,[65] in 1889, Balzar suggested the use of bismuth in the treatment of syphilis. However, it received only little notice until, in 1916, Sauton and Robert used it experimentally with the view of developing its clinical possibilities. These researches were brought to an end by the death of Sauton and the interference of the World War. In 1920, Sazerac and Levaditi [66] took up the task of establishing its value. They finally selected sodium potassium tartrobismuthate as the preparation of choice. They established its therapeutic efficacy, and brought it to the attention of the medical profession. They found bismuth preparations to be more toxic when given intravenously than

63. Wile, Udo J., and Keim, H. L.: Effect of Treatment on Spinal Fluid in Cerebrospinal Syphilis, J. A. M. A. **85**:1269 (Oct. 24) 1925.

64. Stokes, J. H., and Wilhelm, L. F. H.: Tryparsamide in the Treatment of Neurosyphilis; a Study Based on Observation of One Hundred and Fifty-Two Patients for Eighteen Months, Arch. Dermat. & Syph. **11**:579 (May) 1925.

65. Grund, L. J.: The Treatment of Syphilis with Bismuth, Boston M. & S. J. **192**:340 (Feb. 19) 1925.

66. Sazerac, R., and Levaditi, C.: Etude de l'action therapeutic du bismuth en la syphilis, Ann. de l'inst. Pasteur **36**:1 (Jan.) 1922.

when administered intramuscularly. Rabbits tolerated enormous doses intramuscularly, but succumbed to relatively small intravenous doses. Intramuscularly, 50 mg. per kilogram produced no symptoms, 100 mg. produced debility but not death, while 200 mg. killed the animals in two days. Intravenously, 5 mg. per kilogram produced debility, and 10 mg. proved fatal. Other workers have since confirmed this wide difference in toxicity. Good clinical results were obtained by Sazerac and Levaditi. Spirochetes disappeared from a primary lesion by the third day, and the lesion was healed in five days. The Wassermann reaction became negative. In a case of secondary syphilis the spirochetes likewise had disappeared by the third day, and the lesions by the seventh day after the first treatment. In this case, 1 Gm. of bismuth was given in eight doses. At the conclusion of this course, the Wassermann reaction had become negative. The administration of 1.5 Gm. of bismuth in 8 doses to a patient manifesting multiple gummas, some ulcerated, resulted in rapid healing. A black line at the gum margins and mild stomatitis were the only unfavorable symptoms observed. Bismuth was considered to be more effective than mercury and less so than arsphenamine. Aqueous solutions were found to be more irritating than oily suspensions.

The first extensive clinical use of bismuth was undertaken by Fournier and Guénot,[67] who report on its employment in 200 cases. Spirochetes disappeared from chancres rather promptly. They were found occasionally after the second injection and rarely after the third. Secondary manifestations disappeared after one or two treatments. When treatment was started early in the secondary stage, the lesions were aborted. Tertiary cutaneous and osseous lesions responded quickly. Regular treatment in subjects presenting early primary lesions resulted in the maintenance of a negative Wassermann reaction, or, if the reaction was already positive, it became negative after one course of treatment. The latter was true also when the syphilis was in the secondary stage. No serious reactions were encountered in a series of 1,500 injections, though a bismuth line on the gums and mild stomatitis were encountered with some frequency.

Bismuth has been studied intensively, both clinically and experimentally, in this country. Hopkins[68] prefers sodium potassium bismuthtartrate as being the most satisfactory preparation. This contains 54.2 per cent metallic bismuth. In comparing arsphenamine, mercury and bismuth, he administered 150, 30 and 100 mg. per kilogram, respectively, to inoculated rabbits. He found bismuth to be an

67. Fournier, L., and Guénot, L.: Traitement de la syphilis par le bismuth, Ann. de l'Inst. Pasteur **36**:14 (Jan.) 1922.

68. Hopkins, J. G.: Bismuth in the Treatment of Syphilis, Arch. Dermat. & Syph. **7**:745 (June) 1923.

excellent antisyphilitic remedy, standing next to arsphenamine in potency. Clinically, Hopkins administered from 0.1 to 0.2 Gm. of the bismuth salt weekly; having found Fournier's [67] dosage of from 0.2 to 0.3 Gm. triweekly to be too painful to the patient. All cutaneous lesions, including tertiary, responded promptly. Those of the bones responded more slowly. It is possible that the skin lesions would have healed more rapidly with arsphenamine, but certainly not with mercury or iodide. The progress in latent syphilis could be judged only by the Wassermann reaction. In the first group of thirty-one subjects, the Wassermann reaction became negative in only one subject, and this but temporarily. In another group, observed later, an excellent response was noted in many of the "arsenic fast" cases.

Klauder [69] believes bismuth to be a valuable remedy, particularly in those patients in whom a sensitivity to arsphenamine or mercury is found. He has noted a characteristic foulness of the breath immediately preceding severe damage from bismuth poisoning. The toxicity of bismuth when given intravenously is emphasized. No appreciable absorption of bismuth was noted when it was administered by inunction.

Grund [65] has represented the relative values of arsphenamine, bismuth and mercury, respectively, by the figures 10, 7 and 4.

Some of the manifestations of neurosyphilis have responded well to bismuth therapy. Smith and Foster [70] noted that pain, numbness, headache and dizziness are readily relieved. In one subject, meningitis, and in five subjects, hysteroidal manifestations yielded rapidly to bismuth treatment. The improvement, however, was merely symptomatic. No improvement in the status of the infection was observed after two courses of 12 injections each. Green [71] had similar experiences with headaches, convulsions and tabetic pains.

Belding [72] studied the effect of treatment with bismuth on the Wassermann reaction of patients who had been treated previously with arsphenamine and mercury, many of the patients being "arsenic fast." An average of 1.33 Gm. of bismuth was given in a course of ten weekly injections. The average quantitative reduction in the Wassermann reaction was found four weeks after cessation of treatment, in contrast to twenty weeks in another group in which the treatment had been

69. Klauder, J. V.: Bismuth in the treatment of Syphilis; Report of Clinical and Experimental Studies, Arch. Dermat. & Syph. **7**:721 (June) 1923.

70. Smith, W. A., and Foster, L. J.: Bismuth Treatment of Cerebrospinal Syphilis, J. Nerv. & Ment. Dis. **62**:113 (Aug.) 1925.

71. Green, F.: Bismuth in Syphilis, Canad. M. A. J. **15**:163 (Feb.) 1925.

72. Belding, D. L.: The Wassermann Test. IV. The Effect of Bismuth on the Wassermann Reaction in Patients Unresponsive to Arsphenamin, Arch. Dermat. & Syph. **12**:334 (Sept.) 1925.

with arsphenamine. With the bismuth treatment, 13 per cent of the strongly positive, and 63 per cent of the weakly positive reactions became negative. Belding used potassium bismuth tartrate with butyn. This preparation contains from 64 to 69 per cent of metallic bismuth. In ten of sixty subjects, he noted an appreciable general reaction to the treatment; in four the reaction was severe. In three of these latter four cases, the patients were sensitive also to arsphenamine.

Beinhauer and Jacob [73] concluded that the toxicity of bismuth is directly proportional to the rate of absorption, but that the rate of absorption in no way affects the therapeutic action. They recommend the use of a preparation which is slowly absorbed.

Lucke and Klauder [74] found characteristic pathologic changes associated with bismuth intoxication. The kidneys and liver are affected chiefly. In the kidney, swelling of the glomerular tufts and degeneration of the epithelium of the convoluted tubules are found. In the liver the cells are anuclear and stain poorly; occasionally, small areas of focal necrosis are to be observed. Lesions in other organs are inconstant and unimportant.

MERCURY

Of the newer preparations of mercury, flumerin has received some favorable attention in the literature. White, Hill, Moore and Young [75] first described this preparation as a drug useful in the treatment of syphilis. It is a disodium salt of hydroxymercurifluorescein. It contains 32.5 per cent of mercury, is quite stable and has a low penetrating and bactericidal power. A dose of 30 mg. per kilogram is toxic for rabbits, though they usually recover. A dose of 50 mg. per kilogram is always fatal.

Moore and Wassermann [76] report on the treatment of ninety-six patients with flumerin. Chancres healed in an average of twenty-six days with six treatments. Secondary skin manifestations disappeared in an average of seventeen days, but in four additional subjects the lesions were not healed by this means. In twenty of twenty-four subjects, the Wassermann reaction became negative and remained negative

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73. Beinhauer, L. G., and Jacob, F. M.: Relative Absorption and Therapeutic Efficiency of Some Bismuth Preparations, Am. J. Syph. **9**:213 (April) 1925.

74. Lucke, B., and Klauder, J. V.: Histological Changes Produced Experimentally in Rabbits by Bismuth, J. Pharmacol. & Exper. Therap. **21**:313 (June) 1923.

75. White, E. C.; Hill, J. H.; Moore, J. E., and Young, H. H.: Flumerin—a New Mercurial for the Intravenous Treatment of Syphilis, J. A. M. A. **79**:877 (Sept. 9) 1922.

76. Moore, J. E., and Wassermann, H.: The Clinical Results with Flumerin in Syphilis, J. A. M. A. **81**:1848 (Dec. 1) 1923.

in all but three cases. They conclude that the effectiveness in primary and secondary syphilis is excellent, though somewhat less than the arsphenamines, and that it has a marked influence on the Wassermann reaction. The unfavorable reactions were few in number and usually mild. In some patients, however, stomatitis, vomiting and bloody diarrhea occurred. The patients tolerated well a dose of 5 mg. per kilogram on alternate days. A dose of less than 3 mg. per kilogram should not be employed.

Fox, Gildersleeve and Preston [77] have found flumerin to be quite toxic in many instances, so much so that this preparation was abandoned. The dose employed was 4 mg. per kilogram. In those patients who tolerated flumerin, they found it to be more effective than other preparations of mercury they had employed, but less effective than arsphenamine.

Snodgrass [78] noted that primary and secondary lesions yielded less readily and permanently to flumerin than to arsphenamine. The tertiary lesions responded readily to flumerin, but better results were obtained when combined with arsphenamine. On account of the development of toxic symptoms, it was considered necessary to discontinue the use of flumerin in 20 per cent of the cases. In an additional 50 per cent mild mercurialism occurred. The author recommends the use of flumerin, when it can be tolerated, along with one of the arsphenamines, and in place of the older preparations of mercury. Hogan and Robertson [79] concluded that flumerin is particularly beneficial in optic neuritis, choroiditis and iritis. Keratitis is not mentioned.

Cole, Hutton and Sollmann [80] advocate the use of a "clean inunction" method. The ointment is applied in the customary manner, and then the skin surface is cleaned with benzene. The therapeutic value of the inunction seemed in no way impaired by the skin cleansing.

In a study of the skin microscopically, following the application of mercury by inunction, Zwick [81] notes that mercury does not penetrate the skin, but is taken in exclusively by the follicular openings.

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77. Fox, J. C.; Gildersleeve, G. H., and Preston, J. F.: The Value of Flumerin in the Treatment of Syphilis, Arch. Demat. & Syph. **11**:768 (June) 1925.

78. Snodgrass, W. R.: A New Material for the Intravenous Treatment of Syphilis, Lancet **1**:117 (Jan. 19) 1924.

79. Hogan, J. F., and Robertson, J. C.: Flumerin in Ophthalmologic Complications of Syphilis, Arch. Dermat. & Syph. **12**:700 (Nov.) 1925.

80. Cole, H. N.; Hutton, J. G., and Sollmann, T.: The Clean Inunction Treatment of Syphilis with Mercury, J. A. M. A. **82**:199 (Jan. 19) 1924.

81. Zwick, K. G.: A Microscopic Study of Mercury Absorption from the Skin, J. A. M. A. **83**:1821 (Dec. 6) 1924.

SODIUM THIOSULPHATE

In 1920, Ravaut [82] called attention to the usefulness of sodium thiosulphate in arsphenamine poisoning. By using the drug in a large number of cases of poisoning from several of the heavy metals, Dennie and McBride [83] have corroborated its efficacy. They found that moderate amounts are as effective in preventing further damage as are the maximum doses. They recommend the intravenous administration of 0.3 gm. per kilogram of body weight daily for four days, and then on alternate days for as long as is necessary. They report only one failure in twenty-five cases of arsenic dermatitis when following this regimen.

Bugg and Folkoff,[84] using thiosulphate, reported prompt recovery in a child with severe arsenic dermatitis. McBride [85] reported recovery in a child with arsphenamine (hemorrhagic) encephalitis. Both dermatitis and encephalitis are serious events in the course of antisyphilitic treatment, and the recognition of the usefulness of thiosulphate in those conditions constitutes a most important contribution.

Myers, Groehl and Metz [86] found thiosulphate to be more effective in poisoning from trivalent arsenic (arsphenamine) than from pentavalent, or inorganic, arsenic. Excretion of arsenic is greatly accelerated by thiosulphate. From animal experiments, they conclude that the simultaneous administration of arsphenamine and thiosulphate is followed by unimpaired therapeutic action of arsphenamine.

MISCELLANEOUS

Rosen, Müller and Myers [87] have shown that, in all instances, there is a diminution in the number of peripheral leukocytes following the intravenous administration of arsphenamine. This reaction is moderate in those showing no nitritoid crisis, and quite marked in those mani-

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82. Ravaut, P.: L'importance des traitements internes en dermatologie; l'emploi du cacodylate de soude a hautes doses et de l'hyposulfate de soude, Presse méd. **28**:73 (Jan.) 1920.

83. Dennie, C. C., and McBride, W. L.: The Treatment of Arsphenamin Dermatitis, Mercurial Poisoning and Lead Intoxication. Further Observations, J. A. M. A. **83**:2082 (Dec. 27) 1924.

84. Bugg, C. R., and Folkoff, C.: A Case of Arsenic Dermatitis in a Child, Treated with Sodium Thiosulphate, Bull. Johns Hopkins Hosp. **37**:76 (March) 1924.

85. McBride, R. H.: Treatment of Arsphenamin Encephalitis with Sodium Thiosulphate, J. A. M. A. **84**:729 (March 7) 1925.

86. Myers, C. N.; Groehl, M. R., and Metz, G. F.: Therapeutic Activity of Sodium Thiosulphate, Proc. Soc. Exper. Biol. & Med. **23**:97 (Nov.) 1925.

87. Rosen, I.; Müller, E. F., and Myers, C. N.: Studies of the Complex Nitritoid Crisis After the Intravenous Administration of the Arsenicals, Arch. Dermat. & Syph. **10**:316 (Sept.) 1924.

festing such a crisis. Such a change in the leukocytes is considered to be dependent on a reaction on the part of the autonomic nervous system. From this it is concluded that the nitritoid crisis is dependent on a peculiar susceptibility of the autonomic nervous system in those patients who develop a nitritoid crisis. Further observations [88] disclosed the fact that silver arsphenamine did not produce a nitritoid crisis, though a moderate decrease in leukocytes was observed in those patients who previously had reacted to arsphenamine with a crisis. In patients who did not have a nitritoid reaction to arsphenamine, no decrease in the number of leukocytes was to be observed following the administration of silver arsphenamine.

As a result of experimental and clinical studies, Sanford [89] advocates the intraperitoneal administration of neo-arsphenamine to infants in whom the veins are not readily available and in whom intramuscular administration is often followed by abscess formation. His experimental work showed that omental adhesions were formed when the injections were given high in the abdomen, but that administration in the lower quadrants was never followed by permanent changes. His clinical experience with this means of administration was gratifying. Its effectiveness is shown by the promptness with which the bleeding stopped in two cases of hemorrhagic syphilis. The usual manifestations of congenital syphilis also responded satisfactorily. The only untoward effect noticed was a Herxheimer reaction in one infant. The dosage for a 4.5 kilogram infant is as follows: Four injections of 50 mg. in 5 cc. of water at three day intervals followed by four similar treatments at seven day intervals. He considers this an adequate and safe method for the treatment of infants.

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88. Rosen, I.; Müller, F., and Myers, C. N.: The Relation of Silver Arsphenamin to the Involuntary Nervous System and to the So-Called Nitritoid Crisis, Arch. Dermat. & Syph. **10**:607 (Nov.) 1924.

89. Sanford, H. N.: Treatment with Intraperitoneal Injection of Neo-Arsphenamin: Report of 10 Cases, J. A. M. A. **85**:242 (July 25) 1925.

News and Comment

RESEARCH ON SLEEP

In 1924 the Simmons Fellowship was founded at Mellon Institute of Industrial Research, University of Pittsburgh, to carry on a broad study of problems in the promotion and maintenance of healthful sleep. Dr. H. M. Johnson and Mr. G. E. Weigand, psychologists, and Dr. T. H. Swan, physical chemist, have been conducting this research during the past year. Recently, Dr. Carney Landis, physiologist, has temporarily joined the personnel of the investigation. It is announced that from now on there will be two separate Simmons Fellowships at Mellon Institute. One of them will continue the research on the physiologic and psychologic factors of sleep under the supervision of Dr. Johnson. The other Fellowship, held by Dr. Swan, will be concerned chiefly with the subject of bedding materials. This investigational work is being supported primarily for the benefit of the public, and consequently the experimental results will be published.

MISSOURI CONSTITUTIONAL AMENDMENT

The United States Health Service states that the new Missouri Constitutional Amendment providing pensions for the deserving blind in this state brought applications from 5,927. Seventy-five per cent of those classified under optic atrophy was due to syphilis. It was conservatively estimated that 25 per cent of the blindness in these applicants was due either to syphilis or to gonorrhea.

Abstracts from Current Literature

Anatomy and Physiology

A Microscopic Study of the Living Kidney After the Injection of Dyes. J. G. Edwards, Am. J. Physiol. **75**:330 (Jan.) 1926.

The dyes studied come under three categories: (1) those readily eliminated, of the type of phenolsulphonphthalein, in which coloration of the glomeruli appears immediately after injection, followed by a diffuse coloration with the appearance of the dye in the tubular lumina after from twenty-five to thirty-five minutes; (2) those less readily eliminated, as trypan blue, in which the excretion appears to be largely tubular in character, with appearance of the dye in the epithelium of the proximal convoluted tubules; (3) dyes not eliminated through the kidney, as gentian violet. Here no renal staining is seen.

H. E. Eggers.

Liver Cells in the Spleen of a Premature Infant. P. Schnyder, Centralbl. f. allg. Pathol. u. path. Anat. **37**:49, 1926.

In a 7 months infant girl, who lived five days, a group of liver cells 185 by 120 mikrons containing brown pigment, apparently bile, were found in the middle of the front part of the spleen.

George J. Rukstinat.

Histopathology of Hypophysis. H. Kiyono, Virchows Arch. f. path. Anat. **259**:388, 1926.

This is a casuistic study of changes in the hypophysis based on a large necropsy material, the exact number of hypophyses studied not being determinable from the article. The changes encountered are listed according to the portion of the organ involved. In the stalk there were found necrosis, leukocytic and lymphocytic infiltration, hemorrhage and tuberculosis, altogether nine cases. In the anterior lobe there were found four examples of necrosis, three of atrophy and one of ganglioneuroma. In a case of acromegaly the anterior lobe was enlarged, and eosinophilous cells were increased in number. In the pars intermedia there was found a cyst, much larger than the small colloid cysts so frequently seen, and ten cases of lymphocytic infiltration. Collections of neuro-epithelial cells in the posterior lobe were seen seven times. Especial attention was paid to the presence of epithelial cells and pigment in the posterior lobe in eighty-five cases, with positive findings in a large proportion. The epithelial cells are not believed to be misplacements of anterior lobe cells, but are derived from cells of the intermediate zone. The presence of pigment, believed to be proteinogenous in character, bears no relation to the epithelial cells. In a series of fourteen cases of mammary carcinoma, metastasis to the hypophysis occurred in 4 (21 per cent). The author does not believe that the adiposity sometimes seen in mammary carcinoma bears any relation to hypophysial metastasis.

O. T. Schultz.

SPEED OF CORPUSCULAR SEDIMENTATION IN EARLY INFANCY. S. NISHIMURA, J. Pediat. (Tokyo), No. 304, 186 (Sept.) 1925.

Observation was made of blood of rabbits, chickens and seals. Conclusions: 1. Chickens have a greater corpuscular sedimentation speed than either rabbits or seals. 2. In rabbits, the sedimentation is slow up to thirty-five days, and then speed increases. 3. In seals, there is no noticeable change in speed. 4. In chickens, the sedimentation speed is greatest in early infancy, and as they grow older the speed decreases. 5. In rabbits, the male adult has a greater speed than the female.

EXERIMENTAL STUDY OF SEDIMENTATION OF RED CELLS. T. HAYASHI, J. Pediat. (Tokyo), No. 304, 189 (Sept.) 1925.

The experimenter summarizes his findings as follows: (1) Immune serums either accelerate or retard sedimentation; (2) serum of horse, cow, man, goat, and guinea-pig either retards or accelerates sedimentation; (3) serum of rabbits usually accelerates sedimentation of corpuscles in the same species; (4) the corpuscles of rabbits up to 2.5 cc. accelerate sedimentation, but above this amount retard it in the same species; (5) coagulability of blood is not in accord with the speed in sedimentation; (6) when leukocytes alone are injected, the sedimentation speed is depressed and coagulation time is shortened.

KATO, Los Angeles.

Pathology, Bacteriology and Biochemistry

THE EFFECT OF A PROTEIN-FREE ACID-ALCOHOL EXTRACT OF THE PARATHYROID GLANDS UPON THE CALCIUM CONTENT OF THE BLOOD AND THE ELECTRICAL IRRITABILITY OF THE NERVES OF PARATHYROIDECTOMIZED AND NORMAL ANIMALS. LOUIS BERMAN, Am. J. Physiol. **75**:358 (Jan.) 1926.

The experiments of the author show that on injection into dogs of an extract of parathyroid with acid-alcohol at room temperature, there follows an increase of blood calcium and a decrease of electrical excitability of nerves. In the case of parathyroidectomized animals in tetany the symptoms are relieved, blood calcium is raised to approximately its normal level and the threshold of electrical excitability is raised. The last appears to be essentially an effect of the calcium mobilization.

H. E. EGGERS.

THE BASAL METABOLISM OF GIRLS. K. BLUNT, J. TILT, L. MCLAUGHLIN and K. B. GUNN, J. Biol. Chem. **67**:491, 1926.

Comparisons of basal metabolism on the basis of calories per square meter show less variation from the average, among children of different builds, than do comparisons on the basis of calories per kilogram.

ARTHUR LOCKE.

THE EFFECT OF ANTISERUM AGAINST THE SOLUBLE TOXIC SUBSTANCE OF BACILLUS COLI IN BACILLUS COLI PERITONITIS. BERNHARD STEINBERG and E. E. ECKER, J. Exper. Med. **43**:443, 1926.

Intraperitoneal injection in rabbits of eighteen to twenty-four hour cultures of colon bacillus was followed by death in four to five hours, with only a slight degree of hyperemia of the peritoneum. The responsibility of the soluble toxic substance produced by *B. coli* in causing the death of these animals was shown

by the occurrence of death in eight and one-quarter to ten and one-half hours after intraperitoneal injection of 30 cc. of heated supernatant fluid from centrifugalized eighteen to twenty-four hour broth cultures.

An antiserum was produced in rabbits by repeated intravenous injections of supernatant fluid of broth cultures of *B. coli*. Intravenous injection of 10 cc. of this antiserum in rabbits immediately after or one-half hour after intraperitoneal injection of 25 cc. of broth culture of *B. coli* (five times the usual lethal dose) resulted in ten out of twelve animals surviving, whereas all of nine not receiving antiserum died.

McCLURE, Evanston, Ill.

ON ANAPHYLAXIS WITH HEATED SERUM. J. FURTH, J. Immunol. **11**:215, 1926.

Anaphylactic shock may be produced by horse serum heated to 100 C. in guinea-pigs sensitized by the same antigen. Uterine strips of guinea-pigs sensitized to heated horse serum react regularly to an otherwise harmless dose of the same antigen.

S. A. LEVINSON.

THE VIRULENCE OF BACTERIA EXPELLED THROUGH THE INTESTINAL TRACT. G. PERGHER, Ann. d'ig. **36**:81-92, 1926.

The author injected into the respiratory tree of various animals virulent strains of different organisms, and determined their virulency as they were excreted through the digestive apparatus. He found that the organisms passing through the blood streams and eliminated by the enteric route showed definite lowering of their virulence and a pronounced attenuation of their reproducing power. Spores similarly injected and recovered in the enteric juices showed less resistance to heat than normally. He attributes these changes to the chemical action of the blood serum and intestinal secretions and mainly to the phagocytic powers of the organism.

ZAMBARANO, Northville, Mich.

INVESTIGATIONS IN GAS METABOLISM IN CHILDHOOD WITH SPECIAL REFERENCE TO PUBERTY. OSKAR GOTTCHE, Monatschr. f. Kinderh. **32**:22, 1926.

In a comprehensive series of cases, the author determined the specific dynamic effect of a standard diet with special reference to the puberty period. The diet consisted of 200 Gm. of meat and 100 Gm. of bread. It was necessary to determine the basal metabolism before studying the effect of the diet.

The results of the experiments showed that at puberty there is a definite change in the type of response — the so-called puberty reaction. In this period the basal metabolism is definitely increased, but the specific dynamic effect of the food is diminished. The author ascribes this reaction to the changes in the glands of internal secretion taking place at this time.

THE FERMENTS OF THE NURSLING'S STOMACH. KARL WALTNER, Monatschr. f. Kinderh. **32**:37, 1926.

To increase our knowledge of the ferments of the infant's stomach, the author examined the contents of more than seventy stomachs. Examinations were made for acidity as well as for the ferments of chymosin, lipase and amylase.

Various mixtures were first examined for acidity, and then reexamined after being incubated for two hours. The results in terms of p_H were breast

milk, 7.00; sour skimmed milk, 6.90; casein enriched milk, 5.70; milk with butter and flour but no sugar, from 6.9 to 7.00. Practically no ferments were demonstrable in breast milk except lipase.

In well children, even in the very young, chymosin is present. Rennin increases with age and is independent of the acidity of the stomach contents. Lipolytic activity is present in the very young, especially in the breast fed. This does not increase with age, and is undoubtedly due to the ferment present in the breast milk itself. The quantity depends on the amount of fat in the meal. Amylase resembled chymosin.

In children sick with nutritional disease, the chymosin showed little change. Lipase parallels the severity of the disease, and after a severe illness does not return to normal for some time. Amylase conducts itself in a somewhat similar manner to lipase.

GERSTLEY, CHICAGO.

INVESTIGATIONS ON THE REDUCTION COEFFICIENTS OF SMALL AMOUNTS OF THE VARIOUS MONOSACCHARIDES. S. A. HOLBØL, Ugesk. f. Læger. **2**:28, 1926.

The power of reduction of 0.05 to 0.3 mg. of the various monosaccharides (glucose, galactose, levulose and mannose) were compared, using Hagedorn and Jensen's method. If glucose reduction is taken as the standard or 100 per cent, then the equivalents for galactose, levulose and mannose become 71.02, 105.4 and 91.05 respectively.

CONTINUED INVESTIGATIONS ON THE ACTION OF INSULIN AND MUSCLE TISSUE UPON GLUCOSE IN VITRO. CHRISTEN LUNDSGAARD and SVEND AAGE HOLBØLL, Ugesk. f. Læger. **5**:106, 1926.

In a previous paper, it was shown that α-β glucose could be converted into a "new-glucose" when in a solution containing fresh muscle tissue and insulin. In the present paper the authors, by further investigation, have shown that the active substance in muscle tissue does not change α-β glucose into a substance such that insulin can convert it to "new-glucose"; neither is "new-glucose" formed if insulin is first added to the α-β glucose and then the muscle, nor is there any evidence to show that muscle tissue or insulin activate one another so that "new-glucose" can be formed from α-β glucose.

It appears from the experiments that "new-glucose" is formed only when fresh muscle tissue and insulin are added to a solution of α-β glucose simultaneously.

SCHLUTZ, Minneapolis.

NORMAL AND IMMUNE ANTIBODIES IN CHICKS. H. SATO, J. Pediat. (Tokyo), No. 304, 156 (Sept.) 1925.

Brief mention is made of the author's report to the effect that with the increase in the age of developing chicks, there is a concomitant increase in normal hemolysin, agglutinin against immune corpuscles and immune hemolysin, and also in complement and bacteriolysin and agglutinin against colon bacillus.

EXPERIMENTS ON ANIMALS WITH PEROXIDASE PUNCTURE. S. YOSHIMATSU, J. Pediat. (Tokyo), No. 304, 164 (Sept.) 1925.

The author investigated the relation of peroxidase copper reaction to oxidase reaction (Winker-Schnetze) on the leukocytes obtained from peritoneal exudate in the animals which have been successfully punctured for this purpose. The author found simply that the peritoneal leukocytes present negative Sato-

Sekiya peroxidase reaction only after the myelocytic leukocytes in the blood become negative in the animals successfully puncture for peroxidase reaction.

KATO, Los Angeles.

Nutrition

SOME OBSERVATIONS ON THE EXTRACTION OF THE VITAMIN B FROM WHEAT GERM. E. V. MCCOLLUM and H. D. KRUSE, Am. J. Hyg. **6**:197, 1926.

With 95 per cent alcohol containing 1 per cent gallic or tannic acid, satisfactory results were obtained in extracting vitamin B from wheat germ. Similar experiments with other acids yielded only fair or negative results. The extracts were tested by the method described by McCollum and Simmonds (J. Biol. Chem. **33**:55, 1918).

[ARCH. PATH.]

THE NUTRITIONAL REQUIREMENTS OF NURSING MOTHERS. THE EFFECT OF A DEFICIENCY OF THE ANTIRACHITIC VITAMIN ONLY, IN THE DIET OF THE MOTHERS UPON THE DEVELOPMENT OF RICKETS IN THE YOUNG. AGNES H. GRANT and MARIANNE GOETISCH, Am. J. Hyg. **6**:211, 1926.

The findings on experimental rickets as noted in rats are as follows:

Rickets is primarily due to a lack of the antirachitic vitamin, and will develop when a lack of the vitamin is the only deficiency in an otherwise adequate diet.

The diet of the mother is an important factor in increasing or decreasing the resistance of the young to the effects of diets which are deficient in the antirachitic vitamin.

Under ordinary circumstances rickets does not develop in the young of well nourished mothers when a lack of the antirachitic vitamin is the only deficiency in their diet.

The rapidity with which the disease develops and the severity of the lesions depends on the degree to which the mother's reserve of the antirachitic vitamin has been depleted.

After the mother's vitamin reserve has been depleted until the young are made very susceptible to rickets, she can be brought back to normal by increasing the vitamin content of her diet.

The diet of the mother can be made to furnish enough vitamin to prevent the depletion of her reserve of this factor, and to allow her to raise fourth litters that are normal in resistance.

AUTHORS' SUMMARY.

CALCIUM METABOLISM AND THE SYNDROME OF BLUE SCLERAS. TAKAHASHI, Arch. f. Ophth. **115**:206, 1924.

The author reports a family who inherited the condition of blue scleras from the father. Of seven children, four were affected. One showed also the condition of brittle bones frequently associated with blue scleras, having had three fractures, and one child showed a disturbance of hearing which has also been described in such families. Most of the members of the family showed rather marked signs of malnutrition and were of small stature. The four members of the family affected were carefully studied with reference to their metabolism, vegetative nervous system, and blood chemistry. All showed a marked hyperfunction of the vegetative nervous system, recognized by a good many authors as indicating imbalance in the glands of internal secretion. One case showed a markedly increased output of calcium in the urine, with a low calcium

level in the blood, about half of the normal amount. This disturbance in calcium metabolism would point especially to a disturbed secretion of the parathyroid. Pointing to a disturbance of thyroid secretion was the marked increased nitrogen output in the urine and also a low sugar tolerance. This would indicate, however, a hyperfunction rather than a hypofunction, as has been supposed by some to be present, so that from these results at least the parathyroid would seem to be the gland most probably responsible for the condition.

GIFFORD, Omaha.

FEEDING WITH CONCENTRATED BUTTERMILK. HANS WEIL, Monatschr. f. Kinderh. **32**:40, 1926.

As a number of concentrated mixtures have been used with success by various pediatricians, the author thought a mixture of buttermilk with high carbohydrate might also be used. The indications would be cases of poor appetite and cases of obstinate vomiting, in which it might be desirable to reduce the fat.

His mixture consisted of buttermilk, with 2 per cent flour and 13 per cent cane sugar. This gives a content of 3 per cent protein, 1.6 per cent fat, and 0.87 per cent salts. He used the mixture in about sixty cases, and the results were good except in those children who were inclined to diarrhea.

GERSTLEY, CHICAGO.

EXPERIMENTAL RESEARCHES ON ANIMALS AS TO THE INFLUENCE OF UNPHYSIOLOGICAL NOURISHMENT ON THE GROWING ORGANISMS. P. JUNKERSDORF and P. JONEN, Ztschr. f. Kinderh. **40**:1, 1925.

Under a grant from the Rockefeller Foundation, the authors, having already published their investigations on the results of a physiologic diet on puppies, now report a series of experiments on the results of an unphysiologic diet consisting of fresh skim milk and flour. Both as to caloric and protein requirement, the diet is satisfactory. The changes seen in the puppies during life and at necropsy must have been due to a qualitative deficiency; that is, to the absence of fat-soluble A. In the opinion of the authors, the function of this vitamin is that of a catalyzer in the metabolism of carbohydrates.

PERCENTILE DISTRIBUTION OF THE CALORIC VALUE OF FOOD IN PROTEIN, FAT AND CARBOHYDRATES. SYSTEM OF NUTRITION. COMMUNICATION XIX. CLEMENS PIRQUET and RICHARD WAGNER, Ztschr. f. Kinderh. **40**:26, 1925.

A table of foodstuffs is presented for use in diabetes with the value of the protein, fat and carbohydrates worked out in nems.

MOTILITY AND ACIDITY OF THE STOMACH IN HEALTHY AND IN SICK INFANTS. FRITZ DEMUTH, Ztschr. f. Kinderh. **40**:46, 1925.

Many figures and facts are presented, the conclusions of which are to be drawn later by the author.

MECHANOTHERAPY IN THE RICKETS OF INFANTS. HANS WIMBERGER, Ztschr. f. Kinderh. **40**:119, 1921.

The author reports two cases in which mechanotherapy had apparently no effect on the cure of rickets, but the healing was so rapid when cod liver oil was subsequently given that it may be the massage did have some effect.

ALBUMIN MILK-BUTTER-FLOUR MIXTURE. HERBERT POGORSCHELSKY, Ztschr. f. Kinderh. **40**:133, 1925.

A mixture of albumin milk and butter flour was used in 100 cases, with generally good results. This food has a higher caloric value than human milk. It has the same relative amounts of fat and carbohydrates and it has the advantage of being concentrated. Its formula is 5.2 fat, 9.4 carbohydrates, and 2.7 protein. It is particularly indicated in atrophic children recovering from diarrhea.

EXPERIMENTAL RESEARCHES ON THE CONTENT OF VITAMIN C IN COWS' MILK AND ON THE INFLUENCE UPON IT OF DIFFERENT METHODS OF PASTEURIZATION. W. BLUMENBERG, Ztschr. f. Kinderh. **40**:177, 1926.

In this article, Blumenberg protests against the proposal of Meyer and Nassau that guinea-pigs be used in milk laboratories to test the amount of vitamin C in cows' milk because guinea-pigs vary as to their susceptibility to scurvy, and milk which will produce scurvy in guinea-pigs will not produce it in mice. Therefore, no valid conclusions can be drawn as to whether there is enough vitamin C in cows' milk to protect babies.

WATER METABOLISM IN BABIES ON CONCENTRATED FOOD. WALTER BAUMECKER and LUDWIG SCHÖNTHAL, Ztschr. f. Kinderh. **40**:211, 1926.

In a series of infants fed on concentrated food, whole buttermilk or butter meal, it was shown by the authors that some of the infants, after a short fore period of diminished water intake, showed water retention. These children showed a loss of weight. Another group of infants at the beginning secreted water well, and only after a long time showed water retention. In these children their weight first was at a standstill, and then it showed a loss. A third class of infants never showed retention but always secreted normally; they gained continuously. No rules can be laid down because the reaction of infants to concentrated food is individual.

THE SIGNIFICANCE OF COWS' MILK WHEY FOR THE GENESIS OF ACUTE DIARRHEAL DISTURBANCES IN BABIES. FOURTH COMMUNICATION — WHEY AND LACTASE. HEINRICH DAVIDSOHN, Ztschr. f. Kinderh. **40**:251, 1926.

This paper and the five following, are attempts to find what constituent of whey favors the onset of diarrhea in babies. The first approach to the problem is the determination of the influence of albumin, salts and sugar in vitro on the cleavage of milk sugar by lactase. Albumin slows the time and therefore favors fermentation; salts hasten the time. A mixture of salts, sugar and casein hastens the cleavage, which is against clinical experience and cannot be explained.

EMERSON, Boston.

THE AMOUNT OF VITAMIN IN RAW AND IN PASTEURIZED MILK. E. C. VAN LEERSUM, Nederl. Tijdschr. v. Geneesk. **1**:338, 1926.

In the article the question is whether the decrease of the vitamin content of milk after heating is caused only by this heating. The amount of vitamin C only was controlled. In experiments with guinea-pigs, the author found that unheated raw milk did not always suffice in fully preventing scurvy when added to the well-known scurvy-producing food of Holst and Frölich. The guinea-pigs which received raw milk from the retail dealer (which milk was

surely many hours old) all died from subacute scurvy, though they remained alive longer than the animals which obtained food absolutely free from the vitamin C. The animals which received fresh raw milk which was only a few hours old did not show any symptoms. Change from this fresh raw milk to raw old milk, given in addition to the scurvy-producing food, caused a severe form of the disease.

Both kinds of milk were from animals which were on pasture during the best season. The decrease of vitamin C in the dealer's milk is, according to the opinion of the author, caused by the different treatment it has undergone, which all cause an essential increase of the amount of oxygen, to which the vitamin C is very sensitive. He found also that fresh raw milk through which air has been blown for one hour at different temperatures did not prevent scurvy. The guinea-pigs which obtained raw milk through which air had been blown at zero lived much longer than those fed on milk which was treated with air at 37 or 65 C. Pasteurized milk which had been exposed to air for a long time always caused scurvy.

From these experiments, the conclusion might be drawn that it is advisable to use fresh milk, which has been exposed as little as possible to air, and to cool it thoroughly.

ANEMIA, UROBILINURIA AND INTESTINAL HEMORRHAGES IN RABBITS, CAUSED BY AN EXCLUSIVE FEEDING OF COWS' AND GOATS' MILK. E. BROUWER, Nederl. Tijdschr. v. Geneesk. **1**:353, 1926.

Exclusive feeding with milk may produce two kinds of anemia: that caused by lessened production of hemoglobin, and that caused by increased destruction of blood. Feeding exclusively with goats' milk more frequently causes anemia than feeding with cows' milk, which anemia is mostly of the second type, viz., increased destruction. At present, the direct causes of the anemia through increased destruction of blood are unknown. With regard to the problem of the goats' milk anemia, the author tried to produce that kind of anemia experimentally in young rabbits, fed exclusively with cows' and with goats' milk. He succeeded in producing severe degrees of anemia, but not goats' milk type of anemia, though he found some symptoms (urobilinuria and at necropsy capillary hemorrhages in the intestine), which may point in the direction that this experimental anemia is partly produced by an increased destruction.

VAN CREVELD, Amsterdam.

PHARMACOLOGICAL STUDY OF RICE-BRAN EXTRACT. S. YAMAGUCHI and S. ISHIKAWA, J. Orient. Med. **4**:54, 1926.

Patients suffering from beriberi and birds affected with rice disease respond to the use of rice-bran extract. However, the pharmacologic action, especially with reference to the intestinal tract of this treatment, is not fully known.

Experiments by the authors employing oryzanin, oryzanin extract, neutral oryzanin, and neutral oryzanin extract on the intestine of the rabbit lead them to believe that the extract of rice-bran has a slight tendency toward excitation of the normal rabbit intestine, the action seeming to intensify the excitation of the parasympathetic nerves. Oryzanin and the medicament made from the rice-bran have an acid reaction. The inhibitory action they have on the intestinal tract is due to the presence of the acid in the medicament and not to the action of the rice-bran itself. It is impossible to tell, judging by the movement of the intestinal tract, whether the medicament can neutralize the effect of the acid and the alkali.

BARNETT, Chicago.

Prenatal Conditions

REPORT OF A CASE OF ECTOPIA VISCERUM, RACHISCHISIS, MALFORMATION OF THE SACRUM, PELVIS INVERSA, HYPOPLASIA OF THE THORACIC DUCT, AGENESIS OR HYPOPLASIA OF VARIOUS ABDOMINAL VISCERA AND PLACENTA PREVIA. R. MILLS and B. WALPERT, Am. J. Obst. & Gynec. **11**:10 (Jan.) 1926.

Mills and Walpert report a combination of abnormalities occurring in the seven months' fetus of a multipara having a central placenta previa. The upper half of the body was normally developed. The anterior abdominal wall was absent, being replaced by a membrana reuniens; there was complete herniation of all the abdominal contents. The spinal column terminated abruptly at the lumbosacral junction with acute angulation and lateral displacement of a deformed sacrum and a backward displacement and deformity of the pelvic girdle (pelvis inversa). The diaphragm consisted of a thin membranous structure on the right side, but the left half was missing. There was absence of the right suprarenal and the left kidney and their corresponding vessels. The uterus had only one fallopian tube, and there was a persistent cloaca. In addition to these findings there was hypoplasia of the thoracic duct, which the authors make responsible for all of the other anomalies on the basis of congenital ascites due to a disturbance of fluid distribution during growth by the atresic duct. The authors give an extensive bibliography of the major congenital malformations, and believe that theirs has never before been reported.

CONGENITAL HERNIA AT THE LINEA ALBA. H. R. CHARLTON, Am. J. Obst. & Gynec. **11**:103 (Jan.) 1926.

A six-pound male fetus presented at the umbilicus a grape-fruit shaped tumor, 10 cm. in diameter, which contained intestinal coils, gallbladder and part of the liver. Charlton attempted a plastic operation to reduce the hernia, but the child became cyanotic and died at the end of fifty hours. No postmortem examination was made.

ALFRED J. KOBAK.

INTERAGGLUTINATION OF MATERNAL AND FETAL BLOOD IN THE LATE TOXEMIAS OF PREGNANCY. WILMAR J. ALLEN, Bull. Johns Hopkins Hosp. **38**:217, 1926.

The author's conclusions are as follows:

1. The iso-agglutination characteristics of the bloods of 375 normal and of 104 toxemic women and their new-born infants have been studied.

2. There is no evidence that incompatibility is more frequent in toxemic than in normal gestation. Incompatibility between the bloods of mother and infant was present in 20.8 per cent of 375 normal and 21.1 per cent of 104 toxemic pregnancies.

3. There is no evidence of an increased agglutinin titer in the maternal serum of toxemic women.

4. There is no evidence of specific immunization of the mother against fetal corpuscles.

5. The discrepancy between this and previous work is probably accounted for by the size of the series studied. With a small number of cases, the percentage of error and likelihood of coincidence are very great.

6. The study of this series of cases, by the methods used, gives no evidence that the late toxemias of pregnancy have their origin in iso-agglutination phenomena.

THE FETAL SYNTHESIS OF FATS. LAURENCE G. WESSON, Bull. Johns Hopkins Hosp. **38**:237, 1926.

This study is on the question of the placental transmission of fats from the maternal to the fetal circulation, and the fetal mechanism for the transformation of the carbohydrates into fats.

The fat was identified by the amount of precipitate given by the highly unsaturated acids of the fat with bromine, instead of by its iodine number. One group of rats was fed cod liver oil as a percentage of its rations before and during pregnancy, while the other group was fed butter fat for the same period. The fetuses of both groups were removed from the mother just before birth, and were analyzed for the highly unsaturated acids in their fats. No appreciable difference was found between the groups as regards the content of highly unsaturated acids of the fetuses, although a marked contrast was noted between the groups as regards the corresponding values for the mothers.

From his work the author thinks that it is fair to assume that the fetus has been able to synthesize the fatty acids in amount which satisfies its own requirements.

LYTTLE, New York.

CONGENITAL DIAPHRAGMATIC HERNIA. HUGH THURSFIELD, Proc. Roy. Soc. Med., Section for the Study of Disease in Children, **19**:14 (Dec.) 1925.

A boy, aged 6 months, was brought to hospital on account of shortness of breath and loss of weight. The family and past histories were negative. On admission to hospital, the infant seemed perfectly well except that at times his respiration became embarrassed. The dyspnea was growing worse, being present most of the day, with bad attacks after feeding. During the attacks the infant cried, and appeared to be in pain. Cyanosis was noticed at times. The percussion note was impaired over the apex of the left lung anteriorly; below this it was hyperresonant. At the apex, the breath sounds were absent and gurgling sounds were heard. Posteriorly, the note was impaired and breath sounds were absent. The area of cardiac dulness was not well defined. The heart sounds were only heard to the right 1 inch from the midsternal line in the second and third interspaces. The liver lay obliquely, extending across the right side of the abdomen and almost down to the umbilicus.

The roentgen-ray findings were as follows:

The heart was displaced to the right, the gas-filled viscera extended high up in the left hemithorax. Subsequent to an opaque meal, the stomach, dilated and large, lay apparently in the pelvis. It was rotated. From the outset food passed into the small intestine situated in the thorax. The stomach emptied at a normal rate.

FAILURE OF OSSIFICATION AND OTHER ABNORMALITIES OF BONES. DONALD PATERSON, Proc. Roy. Soc. Med., Section for the Study of Disease in Children, **19**:15 (Dec.) 1925.

A girl, aged 5½ years, had slight abnormalities of the face and skull from birth. The face was flat and the bridge of the nose was sunken, the cheeks were prominent and the eyes were slanting. The head was set down between the shoulders. Other members of the family appeared quite normal, and this child was mentally normal. The Wassermann reaction was negative in both the mother and the child. At 22 months of age, the child was brought under observation on account of bony deformities resembling rickets. Roentgen-ray

examination showed slight rickets, but outstanding changes were the fact that the heads of both femora appeared entirely absent and the carpal bones were late in appearing. There was marked genu valgum and the child was undersized. For three and three-quarters years the patient had made no improvement in spite of many treatments. Urinalysis and other examinations were normal.

WILLIAMSON, New Orleans.

CONTRIBUTION TO THE PATHOLOGY OF TWINS. EUGENE STRANSKY, Monatschr. f. Kinderh. **31**:613, 1926.

The article provides clinical and pathologic observations on a number of sets of twins. In one pair, attacks of tetany precipitated strangulation of an inguinal hernia, both children becoming sick and dying on the same day. Another pair suffered from convulsions of unknown origin. Necropsy on one revealed a cyst of the brain; in the other permission for necropsy was refused. The supposition is, of course, that the second child had a similar finding. Other twins suffered identically from eczema and pyodermia, and another pair from severe rickets. The rachitic children ran similar courses until an infection produced a change. The child recovering the soonest from the infection made a good recovery from the rickets, but in the child suffering more severely from the infection the rachitic process remained stationary.

The writer concludes that twins growing from one ovum are very similar, but are not identical in the qualities they inherit.

GERSTLEY, Chicago.

CONGENITAL ELEPHANTIASIS OF ABDOMINAL SKIN. S. KOBAYASHI, Virchows Arch. f. path. Anat. **258**:9, 1925.

In a child dying on the eleventh day after birth of urinary tract infection and meningitis, there was noted at birth a peculiar folded, wrinkled and thickened condition of the skin of the abdomen. Microscopic examination showed the thickening to be due to hyperplasia of the corium. Although the abdominal musculature appeared relatively thin, there was no actual defect of the muscle as occurs in the congenital symmetrical defect of the abdominal musculature described by Stumme, Pels-Leusden and others. The walls of the urinary bladder, ureters and rectum were also thick and hypertrophic. The condition is explained as a developmental anomaly due to some factor acting at that stage of embryogenesis when rectum and bladder are still united in the cloaca, and the anterior wall of the future bladder is in contact with the lower abdominal wall. This corresponds to the 5 to 6 mm. stage of the human embryo.

O. T. SCHULTZ.

Diseases of the New-Born

FEEDING OF THE NEW-BORN. JOHN F. SINCLAIR, Arch. Pediat. **43**:264, 1926.

This is a plea for the general feeding of infants at the breast, with suggestions as to intervals for nursing, complementary feedings, stimulation of the breasts by manual expression if the milk supply diminishes and the advisability of the establishing of breast milk dairies in large cities, as is now being done in New York City, Boston and Detroit.

VON MEYSENBUG, New Orleans.

PROTECTION OF THE NEW-BORN AGAINST TUBERCULOSIS BY THE VACCINE B.C.G. A. CALMETTE, C. GUERIN, L. NEGRE and A. BOQUET, Rev. de la tuberc. **8**:1 (Feb.) 1926.

After reviewing the history of attempts at artificial immunization of animals and man against tuberculosis, the authors summarize the results of their own investigations during the past few years, and come to the following conclusions:

That both animals and man, free from preexisting tuberculosis, may be protected against infection, either naturally or experimentally provoked. This immunity may be brought about by the inoculation, or in the case of very young subjects, by the oral administration, of emulsions of living cultures of bovine tubercle bacilli in which certain original characteristics have been slowly modified by a long series of cultures in a strongly alkaline medium, rich in lipoids (beef bile). The organisms thus modified, called by them B.C.G. (*Bacillus* Calmette-Guerin), have lost their ability to produce tuberculosis, but retain their antigenic properties. This product seems to be perfectly tolerated by all mammals and birds, and even in massive doses does not lead to the formation of reinoculable tubercles.

Their experience with the human subject, up to Jan. 1, 1925, comprises 5,183 new-born infants, mostly of tuberculous mothers, to whom the emulsion was given by mouth. The mortality from tuberculosis in this series, from birth to 1 year, was 1.8 per cent. For the same period the mortality among unprotected infants, similarly exposed to contagion, is in the neighborhood of 25 per cent. The duration of the immunity has not yet been accurately determined, but it seems to last long enough, with reinoculation, to protect the infant, save in the event of massive infection, beyond three years.

They insist that the cultures must be freshly prepared and not held more than ten days. The initial dose should be given at the earliest possible moment, not later than ten days after birth, followed by two doses at two day intervals. Reinoculation should be practiced at the end of the first and second years. The inoculations, they affirm, are absolutely devoid of danger, and febrile or other reactions do not occur.

The technic of the preparation of the emulsion is described in detail, and it is now available to physicians in France through the Institut Pasteur.

SMITH, Ogden, Utah.

Acute Infections

HEMORRHAGIC MEASLES WITH RECOVERY. H. LOWENBURG and A. L. SCHALLER, Arch. Pediat. **43**:73, 1926.

A case of hemorrhagic measles is reported, in which severe toxic symptoms were noted from the beginning. Encephalitis occurred as an early complication. Lumbar puncture yielded a fluid which gave evidence of intense inflammation of the cerebrospinal system. Intraspinous, intramuscular and intravenous injections of immune human measles serum were freely employed. No serum sickness resulted, and after the second intraspinal injection the spinal fluid appeared normal. The course of the convalescence was not shortened, though the hemorrhagic tendency of the measles was apparently favorably effected.

TYPHOID FEVER IN INFANTS WITH SPECIAL REFERENCE TO TYPHOIDAL MENINGITIS. WILLIAM WESTON, JR., and S. X. RADBILL, Arch. Pediat. **43**:160, 1926.

Typhoid fever in children is not uncommon, although it is becoming more so at every period of life, with increasing precautions on the part of municipal

and health authorities. The younger the child the fewer the cases of typhoid fever seen. This may, however, well be due to the smaller chance of exposure and not because of any lesser degree of susceptibility at this period. In the author's series of 100 cases, five were under 1 year of age. Eight deaths occurred in the total series. Of these, four, or 50 per cent, were in patients under 1 year, an indication of the high mortality from this disease existing at this period. The younger the child the more frequent are complications, and death is to be attributed to these in most instances. Otitis and furunculosis were the complications most frequently observed. Hemorrhage and perforation are of uncommon occurrence, especially in infants, but relapse is more common in early than in later life. Of the five cases under 1 year, one patient died with a terminal meningitis due to typhoid bacillus and one appeared to be suffering from a primary typhoidal meningitis.

VON MEYSENBUG, New Orleans.

THE PREVENTION OF SCARLET FEVER. JAMES C. SMALL, M. J. & Rec. **123**:82 (Jan. 20) 1926.

Scarlet fever was known to the medical profession for many years before the era of bacteriology made it possible to search for a specific micro-organism as its causative agent. In 1902, Moser and Pirquet were the first to isolate a streptococcus from patients suffering from scarlet fever and prepared a serum from it which they used in the treatment of the disease. Later in the same year, Miss Tunnicliff showed that the streptococci occurring so constantly in the throats of patients with scarlet fever constituted a particular group, and further showed that, during convalescence patients possessed greater power to fight off infection by this particular streptococcus than normal persons. In 1918, the observation was made that serum from a convalescent subject blanched the rash of scarlet fever round the area of injection. Two groups of workers brought about the solution of the riddle of scarlet fever, Dochez and his workers in the east and the Dicks in Chicago.

The work of the Dicks stands out as epoch-making because of two things: (1) The lack of susceptibility in experimental animals, hence they used human beings for inoculation purposes; (2) they developed a skin test enabling one to pick out susceptible from those not susceptible to scarlet fever.

Therefore, to prevent the spread of such disease as scarlet fever, two plans must be followed: (1) measures must be taken to prevent the spreading of the causative agent, and (2) measures must be taken to render susceptible persons nonsusceptible to the disease.

Having determined those susceptible, they are rendered immune by the injection of graduated doses of the toxin, multiples of the dose employed in the skin test.

The author suggests that medical societies should appeal to the public through the medium of the press, giving definite instruction of the benefits received from the practice of these principles.

WILLIAMSON, New Orleans.

REPORT OF AN OUTBREAK OF MALARIA IN SALINAS, PORTO RICO. ANTONIA ARBONA, Porto Rico Health Rev. **1**:3, 1926.

The study showed that among the 510 cases observed, the majority were suffering from relapses from an old infection. Examinations of the blood of 472 of the patients for the parasites showed *Plasmodium vivax* in 192, *P. falciparum* in 173, *P. falciparum* and *vivax* in five and quartan in three. Among

647 school children 32 per cent were found to have enlargement of the spleen due to chronic malaria. These facts, in connection with the presence of numerous breeding places for the anopheles mosquito, emphasize the necessity of a prolonged curative and preventive campaign. The measures adopted quickly controlled the epidemic, but the existence of four settlements unhygienically constructed on swampy ground threatens the future, and their removal to higher ground is recommended.

LESLIE, Chicago.

THE MANAGEMENT OF SCARLATINAL EPIDEMICS IN SCHOOLS AND INSTITUTIONS. T. STACY WILSON, Proc. Roy. Soc. Med., Section of Epidemiology and State Medicine **19**:1 (Dec.) 1925.

The main difficulty in dealing with scarlatinal epidemics depends on the fact that mild cases often occur, in which there are no characteristic symptoms or signs preceding the occurrence of an infective desquamation. If during an epidemic cases occur in which no contact with a previous case can be established, the presence of someone suffering from scarlatinal desquamation without having had any recognizable signs of the disease must be suspected. When this occurs, inspection of the hands and feet of all inmates is called for and this inspection must be repeated every six or seven days. Inspection must be made in good light and immediately after washing the hands and feet. Other types of nonscarlatinal desquamation must be recognized when in an epidemic isolation of evident cases and inspection of the hands and feet do not stop the epidemic. All cases of minor ailments, such as an attack of vomiting, sore throat, malaise, etc., should be isolated and watched for two weeks or so in order to notice whether desquamation occurs.

WILLIAMSON, New Orleans.

SERUM THERAPY IN BUBONIC PLAGUE. E. RUPERTI-FIERA, Ann. d'ig. **36**:94-104, 1926.

Fifteen patients with bubonic plague were observed and treated by the author in 1924. A report of the cases is given. Four patients were found dead in their homes; three were admitted to the pest-house in coma and too far advanced for any therapy. Of the remaining eight cases, seven recovered under antiplague serum therapy. Response to intravenous injections of the serum was prompt and the lesions healed rapidly and completely. The results were better and the reactions less severe in those cases who had been previously vaccinated against plague. Iodotherapy was tried in one case with poor results. Serum therapy induced severe constitutional reactions, but improvement was almost miraculous in many patients.

Antiplague vaccination, performed with unattenuated, fresh vaccine, has some immunizing value which varies in each subject and is not constant in its effects. Occasionally, disturbing anaphylactic shock is encountered. In many persons stricken with plague, the virulence of the infection is considerably lessened by a previous vaccination. All patients with plague, no matter how severe the condition may be, should receive antiplague serum therapy. It may be given hypodermically or intravenously; the latter is preferable and heroic doses should be administered. Fresh, unattenuated serum must be used in daily intravenous doses of 40 cc. for five or six days. Since constitutional signs of shock always supervene, it is necessary to prepare for this by giving heart stimulants before the injection of serum is made. The author prefers camphor in full doses or even more if indicated and repeated in five or six hours. Follow-

ing the acute reaction cardiac stimulation may be maintained the oral administration of caffeine, strophanthus or digitalis. The suppurating glands, whether primary or secondary, should be incised only when complete liquefaction of the contents has occurred.

ZAMBARANO, Northville, Mich.

IMMUNITY TO DIPHTHERIA. THE USE OF THE ANATOSSINA OF RAMON. I. NASSO, Pediatria **33**:1312, 1926.

In 1925, Ramon reported on anatossina, which he obtained from diphtheria toxin by heating and the addition of formaldehyde. The exact process is not described by Nasso in his review. Anatossina, according to Ramon, retains all the antigenic properties of diphtheria toxin and when injected into horses is capable of producing antitoxin, without any of the dangers of the toxin administration. Nasso quotes Ramon who states that anatossina should be used in preference to the toxin in the preparation of antitoxin.

Because of its nontoxicity, Nasso used it in the immunization of children to diphtheria. He gave a series of two or three injections subcutaneously, of 0.5 cc., at intervals of twenty days. He reports on its use in a series of 120 children, all of whom gave a positive Schick reaction. In 108 of these children, two injections were sufficient to produce a negative Schick reaction, while twelve required three injections to give a negative Schick reaction. In none of the children injected was there a general systemic reaction in a few, a mild local reaction followed the first injection. Schick tests, done eight months later, were still negative on the entire series studied. Nasso feels that the immunity thus obtained is comparable to that followed by the use of toxin-antitoxin and that anatossina has the decided advantage that it does not produce systemic reactions; because of this he recommends its use in place of toxin-antitoxin, in the immunization of children. William Park of New York, in a recent article, stated that he is at present experimenting with Ramon's anatossina. Park's results will be of decided interest and will be anxiously awaited.

DE SANCTIS, New York.

ACUTE ANTERIOR POLIOMYELITIS. W. WÖHRMANN, Virchows Arch. f. path. Anat. **259**:466, 1926.

Wöhrmann describes the cord changes in a case of poliomyelitis in a girl aged 19 years. Death occurred within twenty-four hours of the earliest paralytic manifestations, and the case is considered important because the alterations noted are believed to be the earliest recorded. The changes were limited to the gray matter of the cord and especially to that of the anterior horn. Ganglion cells were degenerated, but there was no neuronophagy at this early stage. There was marked cellular infiltration, with a predominence of polymorphonuclear leukocytes which gave the oxidase reaction. Lymphocytes and large mononuclear cells were also present. The author concludes that poliomyelitis is a true inflammatory process, not primarily a degenerative one, and that in the inflammatory reaction leukocytes are more numerous than has previously been held to be the case.

O. T. SCHULTZ.

CLINICAL AND HEMATOLOGICAL OBSERVATIONS IN VARICELLA. KURT NELKEN, Monatschr. f. Kinderh. **32**:128, 1926.

In an epidemic of varicella, Nelken tried to immunize the unaffected children by inoculating them with the contents of the varicella vesicles. In only a

few of the cases did the inoculation have any effect. In the majority, there was no sign of any local reaction. Those children showing local reaction were by no means protected from the disease, and indeed those with the severest local reactions developed the disease in the more severe form.

With regard to the blood findings, all subjects showed some increase in the plasma cells.

GERSTLEY, Chicago.

THE SPEED OF PRECIPITATION OF RED BLOOD CORPUSCLES IN THE ACUTE INFECTIONS OF CHILDHOOD. II. SCARLET FEVER. LUDWIG BUCHLER, Ztschr. f. Kinderh. **40**:18, 1925.

The author believes that the curve of a speed of precipitation of red blood corpuscles during scarlet fever is so characteristic that with no other help than this, the diagnosis could be made, and that complications can be suspected much earlier by this means than by watching the temperature.

GONORRHEAL ARTHRITIS IN INFANTS. BERTHA HELLMANN, Ztschr. f. Kinderh. **40**:92, 1925.

Gonorrheal arthritis was observed in two infants from three to four weeks of age, one of them born by cesarean section.

THE DICK SKIN REACTION AS A TEST OF IMMUNITY TO SCARLET FEVER. E. NOBEL and H. OREL, Ztschr. f. Kinderh. **40**:96, 1925.

The specificity of the Dick reaction does not seem to the authors to have been fully established, since such a large number of children who have not had scarlet fever react negatively.

OBSERVATIONS IN A CLINIC FOR WHOOPING COUGH. S. MEYER and E. BURGHARD, Ztschr. f. Kinderh. **40**:103, 1925.

The authors report their own observations on 1,064 cases of whooping cough, mostly in infants and very young children. A whoop in this disease at these ages is often lacking and he who waits for this sign, even in older children, may find himself unpleasantly surprised. Dyspnea sometimes occurs as a result not of pneumonia but of emphysema. Small rooms with plenty of veranda space are essential to provide liberal fresh air and to guard against secondary infection. Older children should not be put in with infants because of the danger of secondary infection, nor fresh patients with those nearly recovered because of the psychic influence on coughing; also because of the disturbance of the sleep of the whole ward. Concentrated feeding and skilful nursing are of great value. Venipuncture is praised as a source of relief in complicating pneumonia.

EMERSON, Boston.

Chronic Infections

LATENT TUBERCULOSIS IN CHILDHOOD WITH REFERENCE TO TUBERCULIN REACTIONS, CLINICAL FINDINGS AND ROENTGEN-RAY STUDIES. FREDERICK EBERSON, Am. Rev. Tuberc. **13**:124 (Feb.) 1926.

In a study of 145 cases of juvenile tuberculosis, Eberson was unable to find a definite group of symptoms which would unequivocally justify a diagnosis. Physical examination, likewise, was of slight value except in subjects with frank tuberculosis.

The roentgenogram furnished the most valuable and significant information. Hilum adenopathy with pulmonary foci, together with a suggestive clinical history, warrants a diagnosis of tuberculosis even when symptoms are absent.

Pulmonary foci, often overlooked, were found in 46.5 per cent of his cases, of which 71.6 per cent showed calcification of the focus or of the adjacent intrapulmonary lymph nodes. Peribronchial changes were noted in 5 per cent.

Hilum tuberculosis is characterized chiefly by calcification of enlarged lymph nodes, with extension toward the periphery. Lateral films often showed a significant mediastinal adenopathy not otherwise demonstrable.

The cutaneous tuberculin reactions were in complete accord with the other findings. Seventy-five per cent of all cases gave positive reactions with both cutaneous and intracutaneous tests, while the remainder were about equally divided between the two. Seventy-three per cent reacted more markedly or solely to bovine tuberculin, 26 per cent more markedly to human tuberculin, and 1 per cent to human alone. These tests can be depended on only when made with tuberculin derivatives containing an as yet unknown active principle. The value of positive tuberculin tests in the presence of enlarged mediastinal glands is emphasized by the fact that the same diseases of childhood which produce nonspecific adenopathy, extinguish the tuberculin reaction.

SMITH, Ogden, Utah.

HISTOPATHOLOGY OF SYPHILITIC HYPOPLASIA OF THE TEETH. LOUIS J. KARNOSH, Arch. Dermat. & Syph. **13**:25 (Jan.) 1926.

A historical review is presented, in which it is pointed out that the chronology of enamel deposition, as stated by some authors whose views have been widely accepted, does not agree with the chronology as determined by the writer by compilation. The author studied hypoplasias in extracted teeth with reference to his previously constructed chronologic table. The belief is stated that acute exanthems may explain sharply defined hypoplastic zones and honeycomb notches (though no good evidence is noted to support this view). The chief aberration in the typical Hutchinson tooth is one of gross deformity of the developmental lobes as well as of size. The outstanding defect involves the incisal edge of the middle lobe. All of the lobes are undersized at the biting edge, thus giving the tooth a peg shape. Cross striations or shoulders are not a part of the typical Hutchinson tooth. A Hutchinson tooth is laid down with the enamel and dentine organs not only functioning deficiently, but previously undersized. The general picture is one of fairly intensive hypoplasia in the first year of life with gradual improvement thereafter. Contrary to some of the previous views, the cusp of the first molar is very incompletely formed at birth thus allowing an opportunity for illnesses in the first year to leave their impress on the cusp. Marked hypoplasia in the first year gives rise to the mulberry molar which the author thinks to be characteristic of syphilis, though the possibility is admitted that a nonsyphilitic disease may cause the same deformity. From casual inspection, it is somewhat difficult to distinguish the deformities of the molar occurring as a result of disease in the first year and those resulting from disease in the second year. Presumably only those changes of the first year would be due to syphilis. Apparently in all instances in the study in which the first permanent molars were affected in the first year zone, presumably by syphilis, that part of the crown which is laid down before birth was well formed. Parallel with this observation is the one that the only changes in the first set of teeth which could be attributed to syphilis occurred at the proximal ends of the second molars. This part of

the second molar is laid down after birth. "A time factor of congenital syphilis as a cause of dental hypoplasia seems to be established in the first year of life, the effects coming on suddenly at birth and being concurrent with the stomatitis, rhinitis and other familiar symptoms of syphilis in the new-born."

JEANS, Iowa City.

RELATIONSHIP OF TUBERCULOSIS TO MALNUTRITION IN CHILDREN. HENRY A. REISMAN, Arch. Pediat. **42**:792, 1925.

Incipient, latent, masked and juvenile tuberculous children are not necessarily underweight. Such tuberculosis is not an important cause of malnutrition; malnourished children do not show a higher incidence of tuberculosis. About 64 per cent of contact cases are infected with tuberculosis. The diagnosis of tuberculosis will frequently be missed if one awaits the signal of malnutrition to suspect it.

DISSEMINATED TUBERCULOSIS IN A GIRL OF SEVEN YEARS. JACOB SOBEL and J. GEIGER, Arch. Pediat. **43**:235, 1926.

An interesting case report is given of a child, who was in good health up to the time of admission to the hospital for what appeared to be an acute abdominal condition; an operation for acute appendicitis was performed. A normal appendix was found, but the cecal region was congested. Following operation, a persistent leukopenia, found also before operation, continued, and all tuberculin tests were negative.

Several roentgenograms of the chest failed to show any variation from the normal until three weeks after admission when hilum markings were increased. About two months after admission the child suddenly vomited about half an hour after a hearty meal, complained of severe abdominal pain and of thirst and the abdomen became greatly distended and tense. Pallor, pulselessness, cyanosis and coma followed and she died within two hours. Necropsy showed diffuse miliary tuberculosis and erosion of lymph gland into the right internal iliac artery, with resulting fatal hemorrhage.

VON MEYSENBUG, New Orleans.

SWELLING OF THE KNEES PROBABLY DUE TO THE TOXINS OF TUBERCULOSIS. DONALD PATERSON, Proc. Roy. Soc. Med., Section for the Study of Disease in Children **19**:11 (Dec.) 1925.

The patient, aged 4 years, fell on his knees twelve months ago, causing a swelling which disappeared rapidly though it occurred again from time to time. It was not painful, rest helped but did not cause a complete disappearance. The father died a year ago from pulmonary tuberculosis. At the time of the first swelling, roentgenograms of the chest showed a calcified area in the left mediastinum. The Pirquet test was strongly positive; the Wassermann reaction was negative. The author suggests the swellings were primarily traumatic in origin, and have been maintained by the presence of healing tuberculosis in the child.

WILLIAMSON, New Orleans.

HUMAN TUBERCULOSIS AT DIFFERENT AGES. ANATOMICAL STUDIES. II. TUBERCULOSIS OF ADULT LIFE. W. BLUMENBERG, Beitr. z. klin. Tuberk. **62**:711, 1926.

Of fifty-three cases of healed tuberculosis, it was possible to demonstrate the complete thoracic primary complex in forty-nine cases; in 40 per cent of these, histologic examination revealed true bone tissue. Only two abdominal primary

foci were found. The anatomic studies performed in the technic described in the first communication lead to the following conclusions: The primary pulmonary complexes are not infrequently changed into smooth-walled cavities. The glandular involvement in adults is less pronounced than in the fresh primary complex in childhood. In cases in which no residues of a primary infection can be revealed, the anatomic findings of tuberculous processes are the same as in cases with primary infection. A healed primary infection accordingly does not alter the course of a tuberculosis in adult life, and the adult tuberculosis is conceived not as second or third stage of a childhod infection, but as a disease of its own. With increasing age the indurative changes become more prevalent.

MAX PINNER.

AN UNUSUAL CASE OF BRONCHIAL GLAND TUBERCULOSIS WITH FRACTURE OF A RIB AND INSPIRATORY DYSPNEA. T. STOBER, Monatschr. f. Kinderh. **32**:144, 1926.

A child was brought to the clinic with severe inspiratory dyspnea. Various tests for tuberculosis were negative, though the child did have a considerably enlarged liver. For a time the diagnosis of foreign body in the bronchus was considered.

Necropsy showed that death was due to miliary tuberculosis. The dyspnea was due to the pressure of an enlarged bronchial gland on the right lower bronchus. Fractures in two ribs had resulted from the strain of the respiratory movements on areas of tuberculous osteomyelitis.

GERSTLEY, Chicago.

THE ROENTGEN-RAY DIAGNOSIS OF INFANTILE TUBERCULOSIS. ARVID WALLGREN, Acta Pædiat. **5**:254, 1926.

Wallgren discusses at some length the difficulties of roentgen-ray diagnosis in infancy, and emphasizes the necessity of being familiar with the normal shadows cast by vessels, bronchial glands, etc., at various ages, before pathologic shadows can be properly evaluated.

He feels that the diagnosis of tuberculosis from roentgen-ray findings alone is justified only under two conditions: (1) when the typical picture of miliary or diffuse tuberculosis is present, and (2) when there is evidence of a small, round, encapsulated focus, usually the primary focus. Shadows radiating out from the hilum are the most difficult of all to interpret, for it may be impossible to determine whether a process is confined to the bronchial glands or is spreading into the lung.

Like many other observers, Wallgren finds that as tuberculous processes become inactive, the shadows decrease in size until eventually only a sharply encapsulated area is left. Concerning the nature of the "epituberculous" area, which may persist for months, he has no direct evidence to offer, but he is inclined to believe that it is due to hyperemia and edema of the lung in the vicinity of the focus. By roentgenogram, one cannot distinguish between this condition (tuberculosis with epituberculosis) and a caseous pneumonia.

Perhaps the most interesting part of this study concerns the roentgenographic diagnosis of certain much neglected complications of tuberculosis. 1. Interlobar pleurisy is easily demonstrated by taking vertical plates in two different postures — one with the child bent sharply forward and another with the subject bent sharply backward. In one plate the plane of the pleurisy is perpendicular to the direction of the rays, and shows only diffuse clouding, while the other plate, in which the direction of the rays is almost parallel

to the plane of the pleurisy, shows a small, dense shadow radiating from the hilum. Such a combination is pathognomonic. 2. Bronchial stenosis gives a diffuse shadow in the region of the lung affected, while the remaining portion of lung is emphysematous. The diagnosis is made by the fluoroscope, which shows the mediastinum dragged to the affected side with deep inspiration. 3. Paresis or paralysis of the diaphragm is a rare complication, but may occur when the phrenic nerve is caught in a mass of tuberculous mediastinal glands. The diagnosis is made by the fluoroscope, when the affected side can be seen to remain fixed or even to rise during inspiration.

TWO UNUSUAL CASES OF TUBERCULOUS MENINGITIS. HAEGER, Acta. Pædiat. **5**:422, 1926.

1. A boy, aged 3 years, developed typical symptoms of tuberculous meningitis. Bacilli were not seen in the spinal fluid, but a guinea-pig inoculated with the fluid developed tuberculosis. The meningeal symptoms persisted for two months and then gradually subsided. The child then developed pulmonary tuberculosis from which he was still suffering at the date of the report.

2. A boy, aged 2¾ years, suffering from pulmonary tuberculosis developed typical tuberculous meningitis. The meningeal symptoms lasted only ten days, but facial paralysis and weakness of the legs persisted. One month later the patient died. At necropsy there were found multiple tubercles, as big as a hen's egg, in the brain and cerebellum.

HOLT, Baltimore.

WASSERMANN REACTION IN CHILDBIRTH. I. AVAILABILITY OF RETROPLACENTAL BLOOD. H. BOAS and GAMMELTOFT, Hospitalstid. **69**:49, 1926.

II. IS VENOUS BLOOD OF PARTURIENT SUITABLE? H. BOAS, GAMMELHOFT and K. LICK, ibid., p. 61.

Retroplacental blood may give nonspecific response to serologic tests for syphilis. Positive Wassermann reactions with blood serum obtained in the usual way from parturients may be regarded as dependable. The Wassermann reaction is as dependable in pregnancy and childbirth as at other times.

[ARCH. PATH.]

Internal Diseases

LESIONS OF THE DIAPHRAGM. EDWARD L. JENKINSON, Am. J. Roentgenol. **14**:16 (July) 1925.

Anomalies of the diaphragm are congenital, as are also acquired hernia, evisceration, either with or without a sac, temporary or permanent eventration and thoracic stomach. Hernia is much more common on the left side. Unless the patient is examined from different angles, while in the horizontal position, the lesion may be missed. No food is to be given for at least ten hours before examination.

STULIK, Chicago.

CRETINISM: FOLLOW-UP REPORT OF EIGHT CASES. CHARLES G. KERLEY, Arch. Pediat. **43**:94, 1926.

The eight cases reported were followed for periods varying up to several years into adult life, and show the difficulty of predicting the outcome of any given case. Two patients improved to the extent that thyroid extract dose was reduced to practically nil, with the probability that it would be discontinued

altogether. In others, when there was total absence of the gland, the striking improvement seen at first was not sustained in later life. In those who have reached adolescence, the mental capacity is decidedly defective as shown by the records in each case.

VON MEYSENBUG, New Orleans.

DIAGNOSIS AND TREATMENT OF SPLENIC ENLARGEMENT IN CHILDREN. By SIR HUMPHREY ROLLESTON, Brit. M. J. **2**:1099 (Dec. 12) 1925.

Enlargement of the spleen is a physical sign like jaundice, due to many causes, which in the vast majority of cases are infective, though in many instances, such as in Von Jaksch' anemia and aplastic anemia, it may be impossible to go further than to assume such an origin. The more unstable condition, as regards response to stimulation of the blood forming organs in early life as compared with that in adult life, makes the significance of the blood picture a difficult and therefore an interesting problem.

The spleen and lymph adenoid tissue generally are more prone to active response in children and in general the spleen is more distensible. The author considers these conditions in which the spleen is very definitely enlarged, not including the slight insignificant enlargement so frequently encountered in infants.

A special point of interest in connection with splenic enlargement is in the early stages of the chronic diseases in which it is recognized as occurring, when the other manifestations characteristic of the fully developed disease have not appeared.

The author classifies the condition under the following groups: (1) Those that may be familial (chronic splenomegalic hemolytic jaundice, Gaucher's disease, and congenital syphilis; (2) those associated with changes in the blood picture (anemia, hemolysis, erythremia, leukemia); (3) those definitely infective, whether acute as in enteric, or chronic as in syphilis and tuberculosis; (4) those of tropical origin (malaria, kala-azar); (5) mechanical (growth, cysts, infarcts); (6) associated with hepatic enlargement or cirrhosis.

There is, of course, with this arrangement a certain amount of overlapping, which renders it of little value except as a means of arranging the various conditions in some order or other.

The only interesting comments in this article regarding therapy are those relative to splenectomy and roentgen-ray treatment. Favorable results are obtained with splenectomy in chronic hemolytic jaundice, thrombocytopenic purpura hemorrhagica, Von Jaksch's anemia, Banti's disease (before the liver becomes involved). Less favorable results were obtained in Gaucher's disease, while in the author's experience favorable results were obtained with roentgen-ray therapy in cases of splenomegaly of doubtful origin.

BROWN, Toronto.

TWO CASES OF ABNORMAL OSTEOGENESIS IN THE SAME FAMILY. ERIC PRITCHARD, Proc. Roy. Soc. Med., Section for the Study of Disease in Children **19**:8 (Dec.) 1925.

There is no history of nervous or osteogenetic defect in the family, but the parents were second cousins. There was one older child, aged 21, healthy; one miscarriage before the birth of elder of the two patients, and no evidence of syphilis. The elder of the patients was a girl, aged 17 years, in general health good. She had more than the average intelligence, and was healthy until aged 1 year, when general tenderness developed, which was diagnosed as

"scorbutus." Walking was delayed, the child commenced in a clumsy atoxic manner at the age of 2 years; there was delay and difficulty in starting voluntary movement. At 4 years of age the left leg was one-quarter inch shorter than the right. Lordosis and thoracic and pelvic deformity developed. Skiagrams showed early fusion of the epiphyses. Menstruation commenced at 11 years and the disease which had been progressive up till this time abated. A brother, aged 11 years, was born with contractions and flexions of the lower extremities. There was delay and difficulty in starting voluntary movements. Fractures took place in the long bones, clavicle and patella. External genitals were hypolastic and the testicles were undescended. There was considerable similarity between these two cases, though the girl showed sexual precocity while the boy showed rather the reverse. Although in both cases there was considerable softness and brittleness of the bones, in neither case does the skiagraphic picture present the appearance of rickets. There was no evidence of syphilis and the fact that there was an elder girl of 21 years of age and healthy makes familial disease doubtful. The possibility of pituitary defect is strengthened by roentgen-ray evidence that the pituitary fossa is somewhat enlarged in the girl and somewhat small in the boy.

WILLIAMSON, New Orleans.

CARDIAC HYPERTROPHY IN INFANTS. MOURIQUAND, BERTOYE and CHARLEUX, Arch. de méd. d. enf. **29**:83 (Feb.) 1926.

Cardiac hypertrophies in nurslings have for a long period, under the name of diffuse aneurysms, constituted a composite group related to the most diverse affections. The majority of these, however, are undoubtedly associated with some variety of congenital malformation. Oberndorffer classifies primary cardiac hypertrophy into three groups:

(*a*) Hypertrophy with myocardial lesions.

(*b*) Cardiac hypertrophies with hypertrophy of the thymus — the thymicolymphatic disease.

(*c*) Pure cardiac hypertrophies of congenital origin.

Those cases accompanied by thymic enlargement are the most frequently described. Riensenfeld has made a careful study of five infants, stricken apparently while in good health and without hereditary taint. In these cases, slight cyanosis of the lips and of the extremities was promptly followed by dyspnea and cough, without edema. Percussion showed cardiac dulness increased toward the left. The heart sounds were diminished, but no murmurs were present. The pulse was small, rapid and often irregular. Roentgenoscopy confirmed the findings noted on percussion. Symptoms of cardiac insufficiency rapidly ensued, proceeding in a few days to a fatal issue. Necropsy revealed a general cardiac hypertrophy and dilatation, with special stress on the left ventricle. The endocardium and the valves were normal. The remaining organs were negative, but the thymicolymphatic involvement was very pronounced. In each case there was a great increase everywhere of the lymphoid tissue and, in two cases, marked enlargement of the thymus. In one case there was hypoplasia of the medullary substance of the suprarenals.

Henoch has also noted the coexistence of cardiac and thymic hypertrophy, and Mayer reports a case not only showing this phenomenon but involving similarly the liver, the spleen and the large lymph glands. In casting about for an etiologic factor, various theories have been advanced, without agreement at this time.

The authors report a case under the third group, one of pure cardiac hypertrophy, in an infant, aged 13 months, found in the crèche of the medical clinic for children (Paris). There was a very loud systolic murmur, best heard at the left border of the sternum at the fourth interspace, transmitted especially to the right subclavicular region. The blood examination gave a red cell count of 1,800,000; hemoglobin, 30 per cent, white count normal. Radiograms showed the heart to be enormously enlarged particularly to the right. The baby was intensely dyspneic, the temperature was 101 F., and the skin was of an icteric hue. Within a few days bronchopneumonia developed, and death ensued on the fifteenth day after admission. At necropsy, the heart was found to be twice the size and weight of that in a normal infant of the same age. The kidneys likewise were tremendously enlarged, while histologic examination showed no pathologic change in either these or in the myocardium.

In reviewing the findings, profound anemia alone could account for the loud murmur constantly present during the clinical examinations.

AMESSE, Denver.

INSULIN IN CHILDREN'S DISPENSARIES. A. HEIMANN-TROSIN and H. HIRSCH-KAUFFMANN, Monatschr. f. Kinderh. **31**:536, 1926.

In severe diabetes in a child, the dispensary is not as satisfactory as the hospital, as the children must be watched very carefully and constantly. Tiny infections may throw them into coma. Again, slight changes in insulin dosage may cause profound changes in the blood sugar. The writers report a case to show the difficulty when the child cannot be constantly supervised.

CONCENTRATED FOOD IN PYLOROSPASM AND IN HABITUAL VOMITING. CARL STAMM and OSCAR HERZ, Monatschr. f. Kinderh. **31**:553, 1926.

A plea for the use of concentrated food in cases of obstinate vomiting is made by Stamm and Herz. The authors tried the experiment of reducing breast milk, or cow's milk with carbohydrate, to form one half to one third of the original volume. This was done by heating over a low flame, taking care to avoid boiling. In this way the vitamins were protected.

With mixtures prepared in this way, the authors report considerable success.

CONTRIBUTION TO THE PROBLEM OF STILL'S DISEASE. W. REIMOLD and T. STOEBER, Monatschr. f. Kinderh. **31**:597, 1926.

The writers describe in considerable detail two cases of Still's disease. They note that the spleen is usually enlarged in this condition as is the lymphatic system. An unusual finding in one child, exophthalmus, is explained on this basis, namely, retrobulbar lymph node enlargement. The heart was affected in one child, but this is usually not the case, and the blood shows nothing more definite than a secondary anemia.

These cases are frequently confused with tuberculosis, but tuberculin reactions are uniformly negative.

The two children reported are of interest because the authors were able to isolate *Streptococcus viridans* from the blood of each. For a long while cultures were negative until the observers diluted the blood with a large quantity of bouillon. Then the streptococci were easily isolated.

As the course of the disease is chronic it was possible to observe the effect of a number of types of treatment. None of the usual drugs such as the salicylates had any value. Neither did the roentgen ray, or local applications.

Of unspecific forms of therapy, the best results were obtained by systematic exercises.

In a specific way, vaccine prepared from the organisms isolated from the patients benefited them both as regards their local joint involvements and also their general health.

GERSTLEY, Chicago.

ON FAMILIAL IDIOPATHIC POLYCYTHEMIA IN CHILDHOOD. M. KRETSCHMER, Ztschr. f. Kinderh. **40**:225, 1926.

This is a very rare disease in children of which three cases are here reported. At the age of 4 years, two children began to show ruddiness of the skin and the other had convulsions beginning at the age of 2 years.

EMERSON, Boston.

DIATHERMIC TREATMENT OF SPASTIC PYLORIC STENOSIS IN THE NURSLING. W. TOBLER BERN, Schweiz. med. Wchnschr. **55**:1193 (Dec. 31) 1925.

The author is convinced that even in severe cases of pylorospasm, diathermic treatment is of the greatest benefit. He reports four cases, and concludes that while diathermic treatment of pylorospasm is of great value, it is dependent to a great degree on the proper nursing and feeding.

ELTERICH, JR., Pittsburgh.

Nervous Diseases

AMYOTONIA CONGENITA. J. R. SHUMAN, Arch. Pediat. **43**:225, 1926.

This well-known disease is dealt with in detail as to its etiology, symptomatology, pathologic anatomy and prognosis. Reports are given of cases occurring in two brothers, both dying in early infancy.

VON MEYSENBUG, New Orleans.

LESION OF MIDBRAIN AND PONS. N. HOBHOUSE, Proc. Roy. Soc. Med., Section for the Study of Disease in Children **19**:11 (Dec.) 1925.

The patient, a boy, aged 3½ years, was normal until 17 months of age, when it was noticed the right eye looked inward, then the left arm and leg became weak and at 2 years he could no longer walk. On admission to the hospital, there was complete paralysis of both external recti. Nystagmoid jerkings were noted on attempted movement. There was difficulty in swallowing and very little attempt at talking. Spastic paresis of the left arm and leg was present. The fundi and disks were normal. There was no sensory disturbance. The Wassermann reaction of cerebrospinal fluid was negative. The condition appeared to be slowly progressive. The diagnosis lies between tumor and encephalitis.

INCOORDINATION — PROBABLE ASTATIC-HYPOTONIC FORM OF CEREBRAL DIPLEGIA. C. WORSTER-DROUGHT, Proc. Roy. Soc. Med., Section for the Study of Disease in Children **19**:13 (Dec.) 1925.

The patient, a girl, aged 2 years and 9 months, was admitted to hospital, with a history of being "unable to walk and talk." The patient was late in sitting up, in walking and in obtaining sphincter control. The Wassermann reaction on the blood in April was weakly positive, and on the cerebrospinal fluid was doubtful. Later tests invariably yielded a negative Wassermann

reaction. Patient could stand only when supported, with exercises she learned to walk with assistance; without assistance she staggered and fell. The legs and arms were ataxic. She understood what was said to her, speech was monosyllabic and articulation was indistinct. It was suggested this case was one of the general diplegias in which the cerebellar neurones were affected by degeneration rather than the more usual involvement of the cerebral system.

WILLIAMSON, New Orleans.

ON ENDOGENOUS AND EXOGENOUS FACTORS IN CHARACTER FORMATION. GEORGE A. AUDEN, J. Ment. Sc. **72**:1 (Jan.) 1926.

A twenty-four page discussion of the different conceptions that have been advanced of the relationships between bodily conformation and mental traits is presented. In a diagram the author illustrates his own schema of a fourfold basis of character with two biologic inheritable factors, which he calls somatic constitution and the innate quality of the brain on which intelligence depends, and two exogenous factors which he calls the social and individualistic trends.

BOND, Philadelphia.

RADIOTHERAPY AND RADIODIAGNOSIS OF CEREBRAL TUMORS. GABRIELLE LEVY, Rev. neurol. **1**:550 (Nov.) 1925.

This work is the result of the personal experience of the author and of previous writers. The conclusions are of practical interest and may be summarized as follows: Radiotherapy should be applied to deep, diffuse tumors, particularly to gliomas; to intraventricular tumors, and especially to tumors of the hypophysis. This form of treatment is contraindicated in tuberculomas, gummas and small tumors that are easily enucleated surgically. Before instituting radiotherapy, it is essential to determine whether there is choking of the disks; when the optic nerve is threatened a preliminary decompressive operation should be performed. In the absence of papilledema, roentgen-ray treatment may be applied, beginning with a small dose, and controlling its continuation by neurologic and ophthalmoscopic examinations. If papilledema appears during the course of treatment, the roentgen-ray dose must be diminished or even discontinued. Some authors, including Bremer and Jungling, advise a decompression operation in every case before applying roentgen rays because of the strong probability of the development of a secondary hypertension.

When the location of the tumor is known, the roentgen rays should be centered on the tumor. If the location of the neoplasm has not been determined it is permissable, with caution, to radiate the whole skull by successive fields. There are no indications of the destruction of the tumor except clinical recovery; malignant tumors may recur after radiotherapy as after surgery. When recurrence occurs the roentgen-ray treatment may be repeated. Levy believes that roentgenotherapy, applied with proper precautions, is less dangerous than surgery and will probably acquire a more extended field of application with improvement in technic.

SPINAL HYPERTROPHIC PACHYMENINGITIS AND MEDULLARY CAVITIES. EGAS MONIZ, Rev. neurol. **2**:433 (Oct.) 1925.

The author does not agree with Philippe Oberthur concerning the classification of intramedullary cavities, and discusses the existence of a syringomyelic pachymeningitis in which the syringomyelic cavities are supposed to be

secondary to the pachymeningitis. He is inclined to regard spinal hypertrophic pachymeningitis as an autonomous disease in which the thickening of the meninges produces vascular changes which are the cause of cavity formation. Such autonomy, first described by Charcot and Joffroy, has been confirmed experimentally by Camus and Roussy, and by Lhermitte and Boveri. On the other hand, the histology of the medullary cavities in pachymeningitis is somewhat different from that of the cavities in syringomyelia. The ependymal canal takes no part, at least to any great extent, in the formation of pachymeningitis cavities. The general appearance is different in the two conditions; the contours are irregular in pachymeningitis. The neuroglial reaction is much more marked in syringomyelia. Lastly, the cavities in pachymeningitis frequently affect the white matter.

The author then describes three types of pachymeningitis: tuberculous, syphilitic and one of unknown cause. In cases of pachymeningitis of tuberculous and syphilitic origin the almost constant presence of meningomyelitis due to inflammatory vascular changes renders the tissue less resistant, so that the cavity formation has neither the diffusion nor the characters of the typical cavity; sometimes, even, cavities are absent. When the spinal parenchyma is not affected, the results of compression are more important because of the resistance of the medullary tissue to the meningeal strangulation. The circulatory disturbances that follow explain the cavity formation.

The conclusions reached are: Hypertrophic pachymeningitis of nonspecific nature is the form most connected with cavity formation, and the type of cavity differs from that of syringomyelia. From the therapeutic point of view, surgery, which is often open to discussion in cases of specific nature, is to be recommended in pachymeningitis of unknown origin, especially when localized.

FERRARO, Washington, D. C.

A CASE OF ACUTE LEUKEMIA IN AN INFANT WITH UNUSUAL OCULAR AND NERVOUS SYMPTOMS. AVINIER, Ann. d'ocul. **162**:203, 1925.

The patient was a boy, aged 10 months, whose first symptom was a left facial paralysis. This became bilateral and was followed by vomiting. Then a purulent exudate appeared in the anterior chamber of both eyes; the eyes were not congested, the pupils were unequal and did not react to light. Lumbar puncture showed a rather marked increase in the cell count, chiefly of lymphocytes. Fluid obtained by paracentesis of the anterior chamber was sterile and the cells obtained were chiefly lymphocytes, especially large mononuclear lymphocytes. The exudate re-formed in both anterior chambers. Five days after the child was first seen, a slight fever developed for the first time and the spleen was found to be enlarged. The blood count at this time showed 199,000 leukocytes, principally large and small lymphocytes. The child died one day later. This is apparently the first mention in the literature of a similar exudate developing in the anterior chamber during leukemia, and of an examination showing predominance of lymphocytes in this exudate.

GIFFORD, Omaha.

A PECULIAR NEUROSIS OF THE VEGETATIVE NERVOUS SYSTEM IN YOUNG CHILDREN (ACRODYNIA, ERYTHREDEMA, PINK DISEASE). E. FREER, Jahrb. f. Kinderh. **108**:267.

The author gives a good résumé of the literature on the subject, and adds a complete report of a case, together with a detailed report of the necropsy. This is the seventh case reported by this author. Only a very few other cases

have been reported thus far in Europe, while in the American literature over 100 cases have been reported and more than half as many in Australian literature. The author feels that this frequency of occurrence in certain sections adds to the probability of the disease being due to a specific noxa.

A very good description of the symptomatology and clinical course is given, and the author calls attention particularly to those findings which denote an involvement of the vegetative nervous system. He recalls vasomotor disturbances manifested by severe sweating, cold hands and feet, dermatographia; and the trophic changes manifested by indolent ulcers and gangrene of terminal phalanx of a finger in several cases, and trophic ulcers in other parts of the extremities in a few cases, also by the falling out of healthy teeth and shedding of large amounts of hair, and the appearance in his last case of indolent and deep ulcers on the tongue and in the cheeks, as being undoubtedly due to a neurosis of the vegetative system.

The term "acrodynia" seems to be misleading, for true pain is not present, the discomfort being due entirely to the terrible itching. The name erythrodema is also inapt, because there is no true edema. The author believes the disease is more strictly a "vegetative neurosis," a name which he gave to the disease in a previous article before having encountered the numerous reports by American and Australian authors.

EXTENSIVE TRANSPARENCY IN APPROXIMATELY NORMAL SIZED HEADS AND CONTRIBUTIONS TO THE RECOGNITION OF HYDROMICROCEPHALY. JOHANN V. BOKAY, Jahrb. f. Kinderh. **108**:282.

In a concise article with very instructive case reports, together with necropsy findings and illustrations, the author calls attention to the occurrence of hydrocephalus in infants with normal sized heads and even in microcephalic infants. His interest was first aroused on observing that, in several microcephalic children, he had obtained by spinal puncture a large amount of cerebrospinal fluid under considerably increased pressure. The study of these cases has been much more enlightening since Strassburger in 1909 demonstrated transillumination as a method of determining the presence of hydrocephalus. Since that time he has demonstrated hydrocephalus in four microcephalic children.

He reminds the profession that these findings have been reported by others; and the condition has long been recognized by neurologists. The classical report made by Cruvielhier 1856, and the case reported by Ballantyne 1904 are cited.

Through wider use of transillumination, and eventually also of ventriculography it is to be expected that more widespread recognition of this condition will occur.

PARMELEE, Chicago.

OBSERVATIONS ON THE REACTION TIME OF INFANTS. ALBRECHT PEIPER, Monatschr. f. Kinderh. **31**:491, 1926.

The writer describes an apparatus with which he could ring a bell and get a tracing from an infant determining the time of the reaction. He found the time to be very variable from 0.25 to 0.70 second in the normal waking infant. In sleep the time is longer; even a few seconds. As infants make so many spontaneous motions which complete the experiments, the writer did most of his work on the sleeping child. Premature infants give a longer reaction time than normal infants. Narcotics, such as chloral, phenobarbital and ethyl carbonate, also delay the time, while the effect of bromide was not so definite.

TREATMENT OF CHOREA MINOR WITH HORMONES. J. DUZAR, Monatschr. f. Kinderh. **31**:520, 1926.

In the course of some experimental work with epinephrine, the writer noted that children with chorea seemed somewhat improved. Accordingly he tried the effect of injections of this drug on the course of the disease. His technic consisted of intravenous injections for the first few days, followed by those given subcutaneously. He believes the treatment to be aided by large doses of alkali. With the combination of these two medicaments his results were better than from any other form of treatment.

INVESTIGATIONS ON THE REACTION TIME OF INFANTS. ALBRECHT PEIPER, Monatschr f. Kinderh. **32**:136, 1926.

In well infants the reaction to pain occurs in from 0.12 to 0.70 seconds. This reflex reaction time in infants is about the same as the voluntary reaction time in adults. To make the child cry, a longer time is required, namely, from two to five seconds.

The reaction time is longer during sleep and in premature infants.

GERSTLEY, Chicago.

Diseases of the Eye

CATARACT IN MONGOLIAN IDIOCY. KOBY, Rev. gén. d'ophth. **38**:365, 1924.

The author describes the result of an eye examination of thirty-six mongolian idiots with the slit lamp and corneal microscope. Twenty-two of these showed a peculiar type of cataract, the opacities being just beneath the lens capsule and very much resembling in their distribution and character the opacities seen in myotonic dystrophy. All of those in whom these changes were observed were under 8 years old. The author believes that it has some relation to the onset of puberty, and may be due to a disturbance in the glands of internal secretion.

OPERATIVE TREATMENT OF BUPHTHALMOS (JUVENILE GLAUCOMA). POULARD and LAVAT, Ann. d'ocul. **162**:496, 1925.

In this condition the prognosis has usually been considered very bad, no matter what treatment is adopted. Medical treatment offers nothing, and the use of myotics to reduce the intra-ocular tension seldom prevents the onset of blindness. The author reports the results of eleven cases operated on by sclerecto-iridectomy which were followed from 1913 to 1924. Most of these cases were of the most severe kind. In twelve eyes, the operation was successful in reducing the intra-ocular tension and in keeping it at a safe level. In seven cases a degree of vision sufficient to enable them to carry on their normal activities was obtained. In the others, the operation was done too late. These results in a condition considered by some to be hopeless are encouraging to early operation.

EXPERIMENTAL PRODUCTION OF CATARACTS ON A VITAMIN-FREE DIET. A. VON SZILY and A. ECKSTEIN, Klin. Wchnschr. **4**:919 (May 7) 1925.

In 1923 the authors had reported the production of cataract in young rats whose mothers were kept on a diet free from vitamins. The cataracts produced greatly resembled lamellar cataract, which is seen in young children as the result of malnutrition often associated with rickets. Later observers have obtained less convincing results, and von Szily and Eckstein in this paper

discuss the question whether a slight difference in the diet used by the later investigators will account for these differences. The animals fed by von Szily and Eckstein were deprived of gluten, which was present in the diet supplied by the other investigators. The authors inclined to the belief that there is a hitherto undescribed factor or vitamin in the diet which prevents the formation of cataracts.

EXPERIMENTAL PHLYCTENULAR KERATITIS. SHIN-ICHI-IMMAISHI, Ztschr. f. Augenh. **54**:372, 1925.

The author sensitized his animals by injections of different substances including tuberculin, staphylococcus vaccines and tyramine. After a suitable period a solution of the substance used in sensitizing was dropped in the eye. Lesions very much resembling the phlyctenules seen in human beings followed the instillations in a large number of animals.

GIFFORD, Omaha.

Diseases of the Nose and Throat

ROENTGENOGRAPHIC DEMONSTRATION OF ADENOIDS. C. C. GRANDY, Am. J. Roentgenol. **14**:114 (Aug.) 1925.

The author was able to demonstrate the presence of adenoid tissue roentgenologically. Differential diagnosis of adenoids, postpharyngeal abscess, enlarged pharyngeal tonsils, cervical tuberculosis and malignant infiltration is assisted by careful roentgenology. The author used a Bucky diaphragm, about a 3½ inch gap, a 10 ma., 45 cm. distance and a 10 second exposure.

STULIK, Chicago.

ETIOLOGY OF ATRESIA OF THE POSTERIOR CHOANA. H. VOLOWITSCH, Monatschr. f. Ohrenh. **60**:113 (Feb.) 1926.

In twenty years the author had only two cases of complete atresia of one posterior choana. The patient here reported, a girl aged 16 years, since 1918 complained of a fetid breath and rightsided "catarrh" of the nose. She was not aware of the fact that this nasal passage was completely obstructed. Anterior rhinoscopy disclosed a large, fairly firm rhinolith in the right middle meatus, and bony atresia of the choana on this side. Comparison of the right and left sides of the skull on a roentgenogram showed a small maxillary sinus on the right, with thickening of all its walls as well as of the floor of the right nasal cavity.

Many investigators dispense with the consideration of the etiology of choanal atresia by regarding the latter as an intra-uterine anomaly. Denker and Zarniko hesitate to say that in every instance the condition is congenital in nature, believing that atresia may result from some inflammatory process in the nose. This patient showed no scars in the nose and the mucosa was about normal in appearance. The author attributes the thickenings of the bony walls of the nose to a recent inflammation induced by the presence of the rhinolith. Whether the bony atresia of the choana formed in conjunction with the hyperostosis of the lateral nasal wall and floor, Volowitsch does not say.

GLOWACKI, Detroit.

Diseases of the Skin

ROENTGENOTHERAPY AND DIATHERMY IN BLASTOMYCOSIS. ARTHUR U. DESJARDINS, Am. J. Roentgenol. **14**:14 (July) 1925.

The author feels that the treatment of choice is a combination of surgical diathermy for the removal of thick patches and repeated roentgen-ray irradiation. Nerve blocking is preferred as anesthetic, because the spongy verrucous tissue has rapid seepage, which interferes with local infiltration.

STULIK, Chicago.

GIANT NEVUS. J. D. ROLLESTON, Proc. Roy. Soc. Med., Section for the Study of Disease in Children **19**:7 (Dec.) 1925.

An interesting case of giant nevus with numerous accessory nevi in a girl, aged 3 years, was presented by the author. The large nevus commenced in the upper cervical region posteriorly, and extended outward on both sides, involving the posterior aspect of the right shoulder but leaving the left unaffected and downward to level of the sixth dorsal vertebra. The nevus was pigmented and hairy, and showed several warty growths of the same color as the pigmented skin. Other nevi were scattered over the whole body, the smallest lesions being on the face and scalp. No hereditary or familial history of similar lesions nor any history of maternal impressions were obtained. Rolleston brought the case up for two reasons. 1. To ask suggestions in regard to treatment. 2. The question of maternal impressions, one ingenious theory, as put forward by Bresovsky, was that a giant nevus to occur there must be a twin ovum; that the violent shock produced by the maternal impression causes a reflex contraction of the uterine muscles which breaks up one ovum which is transplanted onto the other, so that a person with a giant nevus bears on his surface a portion of his submerged twin brother.

GRANULOMA ANNULARE. HUGH THURSFIELD, Proc. Roy. Soc. Med., Section for the Study of Disease in Children **19**:14 (Dec.) 1925.

Thursfield presented this case. A girl, aged 3½ years, had had measles, and a family history of rheumatism. Five months previous to admission to hospital, a small, subcutaneous swelling was noted on the right knee. On admission, nodules were noted lying subcutaneously over the left tibia, over the right elbow, along the forearm, and some on the dorsum of the left foot. The nodules were not tender, they were hard, movable and variable in size. Most of these disappeared in a week. However, an oval ring of intracutaneous nodules appeared on the dorsum of the left foot. The Pirquet reaction was negative. There was no reaction to a subcutaneous injection 0.001 Gm. of old tuberculin. Section of one of the nodules showed marked fibrosis and some large multinucleated cells.

WILLIAMSON, New Orleans.

SWIFT-FEER DISEASE. E. JENNY, Schweiz. med. Wchnschr. **55**:645 (July 9) 1925.

The author calls attention to the unsatisfactory nomenclature of this condition, and suggests the term Swift-Feer disease because first described by Swift in Australia and by Feer in Europe; the latter he considers to have given the best description.

In 1914, Swift described this disease under the term of erythedema; Snowball, "raw beef hands and feet," and Clubbe, pink disease.

The first reports from America date back to 1920, when Weston reported eight cases and designated this affliction as acrodynia. Other terms have been proposed, such as, dermatopolyneuritis, pellagroid polyneuritis.

He reports four cases and refers to six cases reported by Feer. He calls attention to the changed disposition of the child and the peculiar knee-chest position, also to the excessive perspiration. Of the ten cases reported, two terminated fatally. Of 167 cases thus far reported there were fourteen deaths, due mostly to pneumonia or sepsis. The duration of the disease averaged four to six months.

Pathologic anatomic findings have only been reported in one case by Byfield. He found in one case changes in the ganglion cells of the anterior horns, gliosis around the central canal, edema of the posterior roots and edema of ischiadicus. The necropsy of Byfield's first patient, similar to the one observed by Feer, macroscopically revealed nothing of importance. The result of the microscopic examination has not yet been reported.

He is of the opinion that the disease is of an infectious nature, and may bear some relationship to influenza, but this is not proved.

ELTERICH, JR., Pittsburgh.

Surgery and Orthopedics

PEPTIC ULCER OF MECKEL'S DIVERTICULUM. E. STUTZ and P. WORINGER, Ann. Surg. **83**:470 (April) 1926.

Heterotopia of gastric mucosa in Meckel's diverticulum is frequent and often the seat of ulcers. These give rise to intestinal hemorrhages and may perforate into the peritoneal cavity with resultant peritonitis. Such bleeding ulcers occur most frequently in infants and children, and the majority of reported cases have occurred in males. The authors present two cases, one in a boy 4 years old, the other in a boy 11 months old. An ulcer in a Meckel's diverticulum was found in each case to have ruptured and caused localized peritonitis. No histologic studies were made.

N. ENZER.

ACTIVE INTESTINAL PERISTALSIS AS AN AID IN THE REDUCTION OF INCARCERATED HERNIAS. HERMAN B. SHEFFIELD, Boston M. & S. J. **194**:876 (May 13) 1926.

The following suggested procedure is so simple that it should be tried before resorting to radical surgical measures:

"The patient is put in recumbent posture with the legs flexed; while the physician endeavors gently but steadily to replace the hernial contents into the abdominal cavity, the patient is directed to swallow mouthfuls of cold water (the colder, the better), which promptly incites active normal intestinal peristalsis. The effect is often almost marvelous — the firmly impacted, totally immobile, apparently lifeless mass, as if by magic, perceptibly begins to gurgle, and gradually, nay, often suddenly, vanishes from the operator's manipulating fingers. It is obvious, of course, that this procedure is not claimed to be a panacea in all cases of incarcerated hernia, but having again and again succeeded in reducing acute hernias, which seemed so near permanent strangulation, by this simple means, I take the liberty of submitting it to the consideration of the general practitioner."

GENGENBACH, Denver.

A Rational Management of Skin Grafts. Ferris Smith, Surg. Gynec. Obst. 556 (April) 1926.

The use of autogenous full thickness (Wolfe) grafts is a very feasible and extremely important method of repairing cutaneous defects. If the type of blood is compatible, isografts may also be used with some degree of success, but the use of noncompatible isografts will always result in failure. A piece of grafted skin acts like a parasite, and its vitality depends on the ease with which an exchange of fluid takes place between it and the underlying surface. This is prevented by the presence of interposed blood, and is seriously interfered with if the grafted skin is contracted, as is usually the case when the ordinary technic is employed. In addition, a certain amount of evenly distributed pressure is required to obtain the best results.

The author, after many years of clinical experience and a good deal of experimental work with various types of grafts, has come to the following conclusions:

1. If possible, the graft should be taken from the same person—the inner aspect of the upper arm or thigh being favorable sites.

2. The graft must be cut the exact size and shape of the area to be covered. (The old idea of cutting the graft large to allow for contraction is wrong.)

3. All fat should be removed from the graft, and it must be sutured accurately on a dry clean fresh surface.

4. A uniform evently distributed pressure must be maintained on the graft, the optimum being about 30 mm. of mercury. (This can be efficiently carried out by the use of the ordinary blood pressure apparatus.)

5. It requires about three weeks for the successful graft to become well organized.

Miller, Chicago.

The Etiology of Hydrocele in Infants. C. Galli, Pediatria **33**:1317, 1926.

Galli has studied twenty cases of hydrocele in infancy, and states that in thirteen of these, there were definite signs of syphilis and a positive Wassermann reaction. In four cases of the series studied, the fluid obtained by puncture of the hydrocele gave a positive Wassermann reaction. Because of the coincidence and the high percentage of syphilis in the series studied, Galli feels that hydrocele is very often a sign of congenital syphilis and should be regarded as such. He quotes many authors who also regard syphilis as a common cause of infantile hydrocele.

De Sanctis, New York.

The Surgical Treatment of Intussusception in Young Children. W. F. Suermondt, Nederl. Tijdschr. v. Geneesk. **1**:1524, 1926.

A report is given of forty patients with intussusception, on whom we performed operations between the years 1908 and 1926 in the surgical clinic of Leyden. In describing the symptoms in detail, the author cites v. d. Ven, who has pointed out that unmixed blood in the bowels is found only in the beginning of the disease. Twice a polypus in the wall of the ileum was found to be the cause of the intussusception. The author also emphasizes the possibility of a relation between intussusception and purpura. In duscussing the treatment, he concludes that internal treatment (massage, enemas) is only justified in the very beginning of the disease. During the operation care has to be taken to prevent chill by reducing the amount of intestine brought outside the abdomen. In the ileocecal form next to the desinvagination, appendicopexia,

as indicated by Hoppe, is done to prevent a recurrence. In the other forms only desinvagination was done. The ileocecal form was found in thirty-five of the forty cases; fifteen children died, that is, 37.5 per cent. The great importance of an early operation is demonstrated by the mortality figures. In patients treated after twenty-four hours, the mortality was three times as large as when the operation was performed within the first twenty-four hours.

VAN CREVELD, Amsterdam.

Miscellaneous

A NOTE ON THE VAN DEN BERGH REACTION AFTER DEEP ROENTGEN IRRADIATION. GORDON CAMERON and HUGO FLECKER, Am. J. Roentgenol. **14**:133 (Aug.) 1925.

The author reports a bilirubin change from 0.7 and 0.8 units delayed direct reaction to 2.5 and 2.8 units biphasic reaction in two cases, eight and six days respectively after irradiation.

STULIK, Chicago.

INTRAPERITONEAL TRANSFUSION IN INFANTS AND YOUNG CHILDREN AND ITS USE IN CONJUNCTION WITH INTRAPERITONEAL SALINE SOLUTION. O. W. HILL, J. T. SMITH and W. R. CROSS, Arch. Pediat. **43**:186, 1926.

Sixteen case reports are given in which intraperitoneal transfusion was made for various conditions. The transfusion is easily and harmlessly administered, and is a valuable adjunct in certain cases. Intraperitoneal injection of saline solution may be combined with the transfusion.

AN ANALYSIS OF SIXTY CASES OF DRUG POISONING. L. M. MURRAY, Arch. Pediat. **43**:193, 1926.

Sixty patients with drug poisoning were admitted to the Hospital for Sick Children in Toronto from 1919 to 1924, inclusive. Of this number, eight, or 13 per cent, resulted fatally. Strychnine played an outstanding rôle, causing one quarter of the cases, one half of the deaths.

Treatment consists of early diagnosis, gastric lavage and purgation, with sedatives or stimulants as required. The vast majority of cases could have been prevented if parents had exercised more care in the measurement of the dosage of drugs, and in the location of drugs and poisonous solutions in the house.

VON MEYSENBUG, New Orleans.

CHRONIC FATIGUE IN THE SCHOOL CHILD. A PSYCHOPHYSIOLOGIC STUDY. PRELIMINARY REPORT. MAX SEHAM, Boston M. & S. J. **194**:770 (April 29) 1926.

The author's clinical working definition is "chronic fatigue is a psychophysiologic syndrome of more than three months' duration, the state of subefficiency manifesting itself in four ways: (1) Feelings of fatigue; (2) actual decrease in the individual's average mental achievement; (3) actual decrease in the individual's average physical strength and endurance, and (4) emotional unbalance."

The child is highly susceptible because: (1) He lacks adequate preparation for his school work, being subjected almost overnight to an artificial regimen with fixed responsibilities and long periods of confinement indoors under marked tension as regards conduct; (2) his inhibitory and coordinating mechanisms

are relatively poorly developed; and (3) his emotional reactions are easily rendered abnormal.

There are tables showing the effect of the maximum amount of work in foot-pounds on pulse and systolic blood pressure, in a child aged 12 years; comparison of anatomic and of objective tests of normal and abnormal subjects; comparison of questionnaires of normal and abnormal subjects, as filled out by the child, mother, room teacher and gymnasium teacher; classification of chronic fatigue in the school child, from a psychophysiologic point of view; measures for the prevention of chronic fatigue, including, of course, all those used in malnutrition classes, but also many helpful suggestions for the cooperation of the public school system; and a daily schedule of rational habits for school children for the orientation of the child's parents.

GENGENBACH, Denver.

SUMMARY OF PROVISIONAL BIRTH, DEATH AND INFANT MORTALITY FIGURES IN THE BIRTH REGISTRATION AREA, 1925. BULLETIN FROM THE BUREAU OF CENSUS, DEPARTMENT OF COMMERCE, WASHINGTON.

The total death rate in 1925, per 1,000 births in children under 1 year of age in the registration area comprising 33 states, was 71.5 as compared to 71.0 for 1924. The lowest death rate in the states was in Oregon with a death rate of 51.2; the highest was in Delaware with a death rate of 90.3. The latter, however, represents a fall from 95 in 1924. The death rate in cities was, in the main, quite low but they were numerous exceptions. In general, it may be seen from these statistics that the lowest death rate under 1 year is in the northwest section of the country, that is, in Washington and Oregon. The death rate in Minneapolis and St. Paul is very low. One would be inclined to think from the statistics shown here that there was not much difference between death rates in the country districts and the city districts. Certainly the figures are illuminating, as they show us how much there is yet to do before we shall have secured the necessary minimum.

GRULEE, Chicago.

CHARITABLE INSTITUTIONS OF PORTO-RICO UNDER THE DEPARTMENT OF PUBLIC HEALTH. E. M. IRVINE-RIVERA, Porto Rico Health Rev. **1**:8, 1926.

There are 700 boys and girls in the government charity schools. These are cared for in two large buildings, with hospital wards and playgrounds. Attention is given to gymnastics and industrial training. The boys are fully equipped to earn a skilled laborer's wage when leaving, and the girls are taught to sew and cook. Provision is made for scholastic training through the second year of high school.

The Institute for Blind Children offers scholastic training through the sixth grade, and instruction in the arts and crafts.

The asylum for the blind gives food and shelter to those who cannot be cured, and those who are not totally blind are given medical and surgical attention, and if sight is fully recovered they are discharged.

THE SOCIETY FOR THE PREVENTION OF TUBERCULOSIS IN CHILDREN. J. RODRIGUEZ PASTER, Porto Rico Health Rev. **1**:13, 1926.

This Society is in no way connected with the Department of Health, but has its enthusiastic endorsement. The Society aims to take children out of homes in which members of the family are suffering from tuberculosis. It

provides a temporary home for them, with good food and fresh air, and finds foster homes for those who cannot be properly cared for by their own relatives.

LESLIE, Chicago.

SCHOOLS FOR SOCIAL WORKERS. MORSIER, Rev. internat. de l'enf. **1**:194 (March) 1926.

Thirty years ago practically all social work was unorganized, and was carried on in a desultory fashion by well meaning amateurs. The necessity for technical training soon became apparent and schools for this purpose are now pretty well scattered throughout America and Europe, the earliest of these being in New York, where it was established by the Charity Organization Society in 1898. Though the curriculum differs somewhat in the various colleges, the object is essentially the same, and there is at present an effort under way to effect some sort of international coordination. A descriptive note on each of the schools is appended.

THE DIMINUTION OF INFANT MORTALITY BY PUBLIC AND PRIVATE EFFORT. INGERSLEV, Rev. internat. de l'enf. **1**:213 (March) 1926.

The high mortality rate among infants in Denmark, where climatic and economic conditions are relatively favorable, leads Ingerslev to conclude that the value of child life is not sufficiently appreciated by the public. Added to this indifference, which seems to prevail in all countries, there is a surprising ignorance among all classes regarding the hygiene of the prenatal and postnatal states. Breast feeding is not practiced universally, as it should be, and the principles of artificial feeding are not understood. The writer believes that, generally speaking, the babies of the poor do not die from hunger but from dirt. It is believed that the infant death rate in Denmark could be lowered in a few years from 75 per thousand to 30 per thousand through the adoption of child welfare measures, conducted by both private and governmental agencies. These would embrace all those activities now carried on so successfully in the United States.

AMESSE, Denver.

THE EFFECT OF DIGITALIS IN WELL AND SICK CHILDREN WITHOUT CARDIAC INSUFFICIENCY. B. SAMET and OTTO TEZNER, Monatschr. f. Kinderh. **32**:1, 1926.

The authors first review the literature, and point out that there is considerable difference between the views of European and American observers. While digitalis is found of value in the heart in pneumonia by many Americans, the Europeans are not entirely convinced of its efficacy. In a like manner the Europeans have not been able to determine the definite and consistent change in the electrocardiogram, resulting from the use of digitalis, which is so well known in American literature.

To throw further light on the question, the authors studied two groups of children, one normal, the other with pneumonia but no signs of heart failure. The medicine was given two to three times daily, and was not stopped until there were noticeable signs of its effect such as arrhythmia. The children were younger, as a rule, than in the American reports, the youngest being about 2 months of age.

The interesting findings were in the group of normal children. It was surprising to note the amount of digitalis these children could tolerate without any effect. An infant, aged 6 months, received 0.1 Gm. of the powdered

digitalis three times daily for ten days with no result. A child, aged 2 years, was given a digitalis extract in 1 cc. doses twice daily for ten days, and three times daily for five days. Other infants received as much as 58 cc. of the digitalis extract by mouth before any effect could be demonstrated.

The infants in the pneumonia group were, on the average, older than the normal babies. A number of these children with pneumonia reacted to digitalis identically the same as the normal ones. Another group seemed hypersusceptible and reacted to even the smallest doses with arrhythmia.

The authors conclude that digitalis is not a drug to be used indiscriminately and as a routine in pneumonia. The effect must be studied in each case. The electrocardiogram is not of great value in children as a guide to the degree of digitalis action, because the change in the curve is not constant. Clinical signs are more reliable. Digitalis should be used only if the cases can be carefully controlled.

GERSTLEY, Chicago.

Society Transactions

ST. LOUIS PEDIATRIC SOCIETY

April 30, 1926

ADRIEN BLEYER, M.D., *President*

LARYNGEAL OBSTRUCTION. TREATED BY INTUBATION, TRACHEOTOMY AND DILATATION. Presented by DR. R. J. PAYNE (by invitation).

Five cases were presented: one of postdiphtheritic stenosis in a child, aged 2½ years; two similar cases in children aged 4 years; one case of chondritis from trauma (adult), and one case of benign papilloma of the larynx (adult).

From his observation of the cases and of many others at the St. Louis Isolation Hospital, Dr. Payne concluded as follows:

1. Tracheotomy should be performed in cases in which reintubation has been done more than seven or eight times. Too frequent intubations result in stenosis.

2. The smallest size tracheotomy tube should be used, to avoid pressure necrosis and to facilitate nasal breathing.

3. Laryngeal dilatation should be instituted early.

4. Progress to larger caliber sounds should be made slowly, as overstretching causes increase in scar tissue and stenosis.

5. No attempt at dilatation should be made without preliminary tracheotomy, because of risk of asphyxiation.

6. Great care should be exercised in passing sounds, as trauma has been the original cause of the stenosis.

7. Decannulation should be preceded by plugging of the tube for a few days.

8. Extensive surgery which might produce edema should be preceded by tracheotomy.

9. No anesthetic, general or local, should be used after initial dilatation. Cases of postdiphtheritic stenosis are poor risks. Termination by cardiac failure or by respiratory infection is always to be feared.

CONGENITAL HEART DISEASE. Presented by DR. A. G. POHLMAN (by invitation).

Congenital heart disease may be separated into three general varieties. The first variety is found in the failure of a transformation of the fetal type of circulation into that of the adult. All postfetal, warm blooded animals enjoy a circulation through the lungs quantitatively equal to that of the general system. Patency of the ductus arteriosus disturbs the quantitative distribution of blood through shunting part of the pulmonary blood through the ductus arteriosus into the aorta. The result is a greater return to the right atrium than to the left atrium, and a functional patency of the foramen ovale. If the ductus is not functionally patent, then the return to both atria is equal and no blood will pass through the foramen ovale.

The second variety of congenital heart comes through imperfection in the septums which split the ventral aorta and the ventricle. When the spiral septum fails to divide the ventral aorta into its two components, the ventricular

septum is also imperfect. The most common variety of this defect is found in a partial or complete atresia of the pulmonary artery. Two cases were shown, one in which the atresia occurred in the proximal segment of the pulmonary artery, and in which all the blood supply to the lungs backed up through the ductus from the aorta. Necessarily, the case was one of trilocular heart, and the child survived only a few hours although perfectly developed in all other respects. The second case presented a complete atresia of the entire pulmonary artery from the ventricle to the aorta. Here five bronchial arteries replaced the pulmonary vessels proper through anastomosis at the root of the lung. In spite of this defect, the child lived for three months with an obviously frequent pulse and rapid panting respiration, probably polycythemia.

The third variety of congenital heart is found in fetal endocarditis, which I believe is more frequent on the right. The specimen shown demonstrates a pronounced involvement of the pulmonary valve. The child had harelip and cleft palate and was seen before the operation. A loud diastolic and systolic murmur but no particular failure in oxygenation were noted. It was suggested at the time that the murmur might in part be due to a moderator band in the right ventricle. The child died a few days after operation from bronchopneumonia. The specimen shows a moderator band, as suspected, placed a few millimeters below the pulmonary orifice. This band may be responsible for some of the loud murmurs, and the time of the murmur will depend on the position of the band. The moderator band is quite normal in the sheep, and is a remains of the developmental concentration of the spongy ventricle in forming the cavity.

Attention was called to the fact that the tight abdominal binder is probably useful in mechanically favoring the closure of both ductus arteriosus and ductus venosus. The serious consequences of a patent ductus venosus was mentioned, particularly at the time of a change in diet from mother's milk to modified feeding, also the possibility of accurate diagnosis of patency of the ductus venosus was suggested.

AMERICAN PEDIATRIC SOCIETY

Thirty-Eighth Annual Meeting, held at Niagara Falls, Canada,

May 31, 1926

FIRST SESSION

J. H. MASON KNOX, M.D., *in the Chair*

PEDIATRIC MATERIAL. Presented by DR. J. H. M. KNOX, JR., Baltimore.

"Is it not possible, however, that as a guild of craftsmen, we have been so occupied with the investigation, diagnosis, treatment and prevention of disease, that we have not given as much attention as it deserves to the quality of the material with which we have to deal, and to the possibility of improving it at its source?"

With this as a proposition, Dr. Knox goes on to show that the pediatrician has the first chance to rescue derelicts and to point out the importance of prenatal care. He calls attention to the inheritance factor in the health of the child, and shows that longevity of the parents is often associated with

reduced infant death rate. There is grave danger in the reduction in the size of families among the well-to-do and scientists. The problem of the feebleminded who propagate their kind is a serious one, and the number of such persons is on the increase. He cites the results obtained by segregation of cretins in the valley of Aosta in northern Italy, and feels that such measures are the natural ones for dealing with other classes of feebleminded. "The hope of the race lies in eugenics and in euthenics."

The environment during pregnancy, labor and the early postnatal life is of great importance. In the latter field especially, much has been accomplished during the last twenty years. "The salvage of human life has taken place for the most part among the unfortunate."

Improvement in environment enables the individual to approach the potential capacity of his inheritance. Eugenics and euthenics are interdependent.

"The only practical method of improving the human stock is by selection." For this purpose, education is better than legislation. The duty of the pediatrician is plain. He should seek to better both heredity and environment.

THE USE OF AUTOGENOUS VACCINE IN THE TREATMENT OF SOME INFECTIONS OF CHILDHOOD. Presented by DR. LEON VELASCO BLANCO (by invitation), Buenos Aires, Argentina.

The use of vaccines as a means of therapy in various disease conditions is well known, and is a procedure which has been widely practiced in many countries. Regarding their efficacy, there is much division of opinion; some physicians favor their use and others have found them practically without value. The experiences with their use and the results obtained in pediatric practice in Buenos Aires have, on the whole, been very good.

For the past two years or more, the treatment of infectious diseases by means of autogenous vaccines has been extensively used in the pediatric clinics of Buenos Aires. The conditions in which they proved particularly efficacious were gonorrheal infections, pneumococcus empyema, and pyelocystitis.

Some experimental work of Dr. Luisa Bonacorci showed definite biologic differences between the gonococcus found in vulvovaginitis of female children and that found in the adult. These differences are particularly manifest in agglutination reactions and complement fixation.

The autogenous vaccine was prepared by taking cultures of the gonococcus in each individual case and also a portion of the accompanying flora. This generally included *Bacillus coli,* streptococci, staphylococci and occasionally *Bacillus proteus.* The material obtained, after suitable preparation of the genital tract, was added to blood agar or albumin agar and incubated for twenty-four hours. From this culture many transplants were made and the gonococcus finally isolated. The final product is in the form of a sterile emulsion. The content of an ampule containing approximately 1 cc. of the emulsion is injected at intervals of from twenty-four to forty-eight hours, depending on the degree of reaction produced. The injections are generally given in series of six with an interval of eight days in between. Fairly rapid and, with few exceptions, constant and permanent improvement followed this procedure.

In pneumococcic empyema the autogenous vaccine therapy was not employed as a curative therapy, but rather with the object of lowering the virulence of the pneumococcus in this condition and thus making early operative procedure more safe. The favorable experience in a fairly large number of cases

would indicate that the use of autogenous vaccine in pneumococcic empyema is not only desirable but definitely indicated as a procedure which will in every way favorably influence the prognosis of the case.

In pyelocystitis the autogenous vaccine therapy has been most successful in severe acute types, many chronic types and those resistant to the usual forms of treatment. The presence of agglutinins observed in all the cases after the injection of autogenous vaccine, notably the coli vaccines, would seem to point to its specific action.

The series forming the basis of this report is rather small, but the results obtained with this form of therapy were so constant that it seemed worthwhile to make a preliminary report.

MEASLES IN PRIVATE PRACTICE AS MODIFIED BY THE USE OF IMMUNE SERUM. Presented by DR. ROWLAND G. FREEMAN and DR. R. G. FREEMAN, JR. (by invitation), New York.

In contemplating the administration of measles immune serum, there are two possibilities to be considered. First, the occurrence of the disease may be prevented by the development of a passive immunity lasting from three to six weeks. Second, we may obtain a modified form of the disease which gives an active immunity lasting, as far as we know, as long as that conferred by the ordinary noninjected case. It is the purpose of this paper to show that the first type can never be depended on, and in the majority of cases is not desirable.

The cases we desire to present are cases belonging to the second class, in which the children have been thoroughly exposed and have then been given immunizing doses of serum intended to allow development of the disease, so as to obtain a permanent immunity through a mild attack of measles.

The results on children in institutions showed 85 per cent complete protection. In the 220 private cases on which there were accurate reports, 42 per cent showed modified measles; in 6 per cent the course of the disease was unmodified, and in 52 per cent there was complete protection.

In judging the results of a series of institutional children, the definiteness of the exposure can never be accurately determined, and it is safe to say that a good many of the children recorded as completely protected were never exposed.

It is possible that differences in results may be due to differences in the potency of the serum, which may vary in direct proportion to the severity of the disease.

It has been the custom of the New York Health Department to pool six or seven different bleedings, whenever this was possible.

It has been attempted to abort the disease by the injection of 20 to 30 cc. of serum during the period of invasion, but there have been no results that would indicate any benefit from this measure.

The patients presented, on whom an attempt was made to obtain an immunization or a modified form of measles, were all given 6 cc. of an immune serum, prepared by the laboratories of the New York Department of Health, and obtained from persons who had recovered from measles, on about the tenth day after the onset.

In the first case tabulated, 20 cc. was given to a child in whom the rash was just appearing, without any apparent modification of the subsequent course of the disease.

The type of the disease obtained when measles occurred after the administration of this dose of 6 cc., in almost every case, showed a marked modification of what one sees when no serum is used. The characteristics of these modifications are that no symptoms are usually noticed until the rash comes out. At this time the child has an elevation of temperature, often with the presence of Koplik spots in the mouth, with much less cough than measles cases usually have, but in all the cases we have observed, there have been catarrhal symptoms. In most of these cases the temperature is normal the following day, and there are no further symptoms.

In analyzing this small number of cases, twenty-two in all, to determine on what day after exposure the best results may be obtained, we find that in the total number of twenty-two cases there were six cases with no measles, and sixteen cases in which a modified form of measles occurred. Of the eight cases injected the day after exposure, three cases had no measles while five had modified measles.

Of those patients injected on the second day after exposure, three developed measles, but the first two of these occurred so late that they were probably due to subsequent exposure in the school in which the disease was rampant. One developed on the eighteenth day, one on the forty-first day, and one on the fourteenth.

Of the seven patients injected on the third day after exposure, three developed no measles and four developed modified measles.

The one subject injected on the fourth day developed measles in thirteen days. The two patients injected on the fifth day had a very mild attack of measles on the nineteenth day.

One patient injected on the seventh day had a markedly modified measles.

This table seems to indicate that a late administration of the serum is less apt to prevent measles from occurring than an earlier administration, which is in accordance with what one would suppose.

Of the cases which we have tabulated, we are indebted to Dr. Herbert B. Wilcox and to Dr. Nathaniel R. Norton, for the use of the cases injected by R. G. Freeman, Jr., for them.

I think we may conclude from this that, while the use of convalescent measles serum is a valuable measure in the modification of the disease, and in the prevention of its complications, that it cannot be depended on to prevent the occurrence of measles, no matter at what stage of the incubation period it is given, nor in what amount, up to 10 cc.

DISCUSSION

DR. KOPLIK: The more I see of measles the more I am afraid of statements concerning contagion. Dr. Chapin of Bridgeport says exposure means nothing unless it is direct. We read a great deal in the literature about immunity in relation to measles, but I dare say that often we do not know the exact immunologic history. Then we have cases of abortive measles — Koplik spots and slight fever — and we have a number of cases with double and triple attacks, so I wish to emphasize the fact that statistics are very fallacious. A child may have been in the same ward with measles cases; the child may merely have run into the ward and out again, and that is put down as exposure. But that is not exposure. There must be direct contact, as by a thermometer, spoon, foods, plates, etc., when a nurse or someone in contact with measles cases comes in contact with another child. These are the cases that determine how much the serum represents.

DR. HERRMAN: I do not think there is any doubt that serum is useful in institutions in which babies are not well nourished, and also in private practice when babies are below par, but, so far as the problem affects the community in general, I doubt whether convalescent serum is of great value. The reason is plain. There is a comparatively small number of cases in which the exposure is known.

The passive immunity conferred by the serum is of short duration. The control of epidemics of measles requires active immunization in infancy. The situation is similar to that in diphtheria, although antitoxin is of great value, it is being superseded by active immunization with the toxin-antitoxin mixture. We should also bear in mind that in addition to the humoral immunity there is possibly a cellular or tissue immunity.

DR. FOOTE: It is interesting to notice the variations in natural immunity. I made it a practice to inject a number of children who were in the late prodromal stage of measles with blood from another member of the same family who had just recovered from measles. This blood in the amount of 15 cc. was injected into the buttock of the patient as soon as Koplik spots began to appear. In one group, four of the five children so injected had very mild attacks, while one had a severe attack with pneumonia. But it is notable that while four children who were injected had these mild attacks, two other children of the same families had mild attacks *without any injection* of recovered blood. So it would appear that there are many variations in natural immunity to measles. These natural variations in immunity in this disease are commonly seen, and make it difficult to draw conclusions as to the efficiency of any methods of preventive treatment.

DR. KERLEY: After treating measles for many years, during the past winter I saw my first fatal case in a child aged 3 years, in which attempts had been made to reduce the temperature by cool baths.

For five days the measles rash had been trying to materialize, and during this time the child had been sponged with cold water because of the family fears of an elevation of the temperature. The temperature had not been allowed to rise above 101.5 F. When I saw the child Koplik spots were present, and there was some rash under the ears and around the neck. The child presented the clinical appearance of anaphylactic shock and died a few hours later, with all the appearance of a measles rash struggling to come out. The case seemed to represent what is sometimes described as suppressed measles. It was evident that the cold bathing was sufficient to prevent the disease from going through its usual cycle.

DR. SCHICK: I can only confirm, that the use of convalescent measles serum has great value in fighting measles in institutions. Even if the patient should develop modified measles, the injection has been helpful. An interesting fact is that the incubation period of modified measles is prolonged. In case we cannot obtain an adequate supply of convalescent serum, we use 30 cc. of adult serum, and have had satisfactory results. This amount of serum corresponds approximately to 90 to 100 whole blood. We, therefore, do not immunize children who previously have been transfused with a sufficient amount of blood. The use of adult serum in measles prophylaxis is a great advantage to the general practitioner in case he cannot obtain convalescent serum, as it is usually possible to get the serum from a member of the family. The only disadvantage of using adult serum or whole blood, is that diseases can be transmitted in this way, particularly tuberculosis. I know of two cases of tubercular infection caused by the use of convalescent serum (Kundratitz).

The serum had been taken from a child with a positive Pirquet test, although otherwise healthy.

DR. GRULEE: I had the opportunity to use, parallel with convalescent measles serum, the goat serum of Tunnicliff, and, so far as the prevention of measles in the ward was concerned, there seemed to be no difference between the goat serum and the measles serum. The goat serum gave just as much protection as the convalescent serum, but it seemed that with the goat serum there was a tendency to anaphylaxis.

NEUROMUSCULAR DYSFUNCTION OF THE BLADDER AS A CAUSE OF CHRONIC PYELITIS IN CHILDREN. Presented by DR. HENRY F. HELMHOLZ, Mayo Clinic, Rochester, Minn. (This article will be published in full in a later issue.)

THE OCCURRENCE OF PYURIA IN MALFORMATIONS OF THE URINARY TRACT. Presented by DR. I. A. ABT, Chicago.

The author has observed a number of children with protracted pyuria, in whom malformation of the bladder, ureters or kidney were demonstrated by cystoscopic or roentgenographic examination, or occasionally at necropsy. This etiologic factor as a cause of chronic pyuria has received scant attention in the pediatric literature. However, attention has been called to it by Gerstenberger and Wahl, Wolfgang, Courtin, Hyman, Clinton J. Smith, Bugbee and Braasch. Courtin has reported three cases of pyuria associated with malformations of the bladder and ureters.

A number of lantern slides were presented which illustrated dilatation of the ureters arising from various sources. The case histories showed that the dilatation might be congenital in origin or arise from spinal cord lesions, as has been pointed out by Braasch and by Ransohoff. It might result from infection with inflammatory changes in the ureter and ensuing obstruction.

The case histories further illustrated the various phases of obstruction and infection in malformations of the urinary tract in children. Pyuria was the outstanding manifestation in all instances. Other symptoms complained of were dysuria, vomiting, chills and fever, pallor, suprapubic pain, incontinence of the urine, and frequency of urination. In all of the cases the pyuria was protracted, and did not improve under the usual medical treatment which was continued in some instances for weeks or months.

In conclusion, the author points out that congenital or acquired malformations of the urinary tract causing dilatation lead to urinary stasis. When stasis occurs, infection is likely to ensue. The pyuria which results runs a protracted course, associated with fever and emaciation, and progressive degeneration of the urinary organs. Every child with protracted pyuria and fever, in whom the condition fails to respond to the usual methods of treatment within a reasonable time, should be subjected to cystoscopic and roentgen-ray examination by a urologist.

DISCUSSION

DR. CARR: The causative factors of pyuria have been thoroughly studied with reference to blood stream infection, mechanical interference with drainage, etc. In determining the more simple cases of pyuria, we have recognized that we may have certain anomalous conditions which are not always easily treated, and which require both cystoscopic and roentgen-ray examinations for diagnosis.

Bugbee and Wollstein, in 4,903 necropsies made by Dr. Wollstein, found 2.3 per cent of anomalies of the urinary tract, and Bugbee states that: "Obviously an infection superimposed on such a condition would not clear up by ordinary methods of treatment."

Interesting specimens were presented through the courtesy of Dr. Plaut, pathologist at the Woman's Hospital. Two brothers, born one year apart, showed the same malformation of kidney and penis. The mother had some anomaly in the pelvis of one kidney; the character of this anomaly was not determined, because the woman will not be subjected to further pyelography.

The first boy, 39 cm. long, showed signs of immaturity. The left kidney measured 5 by 2.7 by 2.2 cm. The pelvis was somewhat large, otherwise normal. The ureter and its opening into the bladder was normal. The right kidney measured 5.2 by 2.9 by 2 cm., the lower half being much thicker than the upper one, and on its anterior aspect is a cyst nearly 2 cm. in diameter. This kidney contained *two separate pelves,* the upper one being small, the ureter originating from it; it appeared normal. The lower pelvis corresponded to the before-mentioned cyst; at its lower pole it was continuous with the other ureter; this was twice the size of the first one. The orifices of both ureters were very near each other; the upper one had a normal small round opening; the lower one opened into the bladder with a slit which surrounds the first one laterally and a little upward.

Microscopic sections of the kidneys showed very irregular pictures, with superfluous undifferentiated tubules. There was a hypoplasia of the penis. All the other organs were normal.

The second boy was 50 cm. long, and mature. The kidneys measured 7.5 by 3.55 by 2.2 cm. On the right side one ureter was found; on the left side there were two ureters originating at a distance of 2 cm. from each other and from the hilum. They apparently united under the lower pole of the kidney, being surrounded by a sheath of connective tissue. The kidneys on both sides had two pelves. The upper pole of the urinary bladder was unusually large. There was retention of both testicles, and also hypoplasia of the penis.

DR. KOPLIK: There are a great number of cases of pyelitis in children, and the question of the child being perfectly normal is important. If the child is absolutely normal, the tendency of the disease is to clear up, but if there is the least abnormality, congenitally or otherwise, there is a chronic pyuria which it is almost impossible to cure. In these children, the condition runs along for years. I have had a number of these patients operated on, under the guidance of Dr. Beers. What I fear most is when the urologist suggests that these cases be injected through the ureters, especially when the catheter could not be passed immediately. I am inclined to think that patients without abnormalities vaccinate themselves, the temperature drops and becomes normal, whereas in the abnormal cases it is impossible to secure proper drainage. It is a question whether these dilatations are congenital or acquired.

DR. RICHARD SMITH: I have nothing new to add to what Dr. Helmholz has said in presenting this interesting subject. I wish to emphasize two points. First, when we investigate the children with chronic pyelitis we find that a large proportion of them show some abnormality of the urinary tract. It is, therefore, important that a cystoscopic examination be done in every child with persistent pyuria. Second, it is important for us to bear in mind that no amount of medical treatment will effect a cure in children who have an inadequate drainage of the kidney. Cure is accomplished only by relieving the mechanical condition.

DR. CROTHERS: The question of bladder innervation is very complex. The injuries to the spinal cord during the war threw much light on bladder function. Head and Riddoch's work in particular is worth studying. At least two types of "cord bladder" exist. First the familiar "atonic" bladder with almost

inevitable infection, and second, the "automatic" bladder which empties at a relatively fixed pressure. This second type does not become infected, as a rule.

Another point, brought out by Orr and Rows, is that the nervous system, including the cord, can be injured by lymphogenous infection. In this way it is conceivable that chronic urinary infection may play a rôle in the production of incontinence.

The further study of the subject should take due account of the primitive nature of fetal nerve tissue.

Dr. Cowie: During the last three or four years, I have been interested in the bacteriophage treatment for pyelitis. We have had considerable success in a certain group of cases by using a bacteriophage lytic for the organism causing the infection. It was a long time before we were able to obtain an active bacteriophage for therapeutic purposes. We succeeded in isolating a bacteriophage from the sewer as it flows from the end of the pipe into the river at Ann Arbor. This bacteriophage on single or double filtration was active for the colon dysentery and typhoid groups.

By giving small subcutaneous doses of this bacteriophage (2 or 3 cc.) on alternate days for three doses, in twenty-four to forty-eight hours the urine often became sterile. We hope from the immediate results obtained in some cases that we are going to have considerable success with this method of treatment but, in the course of time, some of these patients had recurrences while others continued sterile.

The bacteriophage will unquestionably sterilize the genito-urinary tract in a goodly percentage of cases of colon infection, but if the condition causing or favoring the infection still remains, there will be reinfection. The bacteriophage merely sterilizes for the time being, the same as arsphenamine sterilizes but does not protect against future infection. When there is no anatomic defect bringing about poor drainage in child, infant or adult, the bacteriophage will terminate the disease in a large percentage of the cases. The sterilization may be very prompt, or not until several days after the last injection. Thus far, we have not been able to obtain a satisfactory bacteriophage filtrate for the coccus group of organisms. Such a bacteriophage, to be effective, we think must be autogenous, that is, isolated from a coccus infection case, and the virulence stepped up.

Dr. Knox: Some weeks ago, there was brought to me an infant girl, aged 14 months, who had had persistent pyuria for several weeks. There were the usual symptoms of high, irregular temperature, loss of appetite and weight. She had been treated at intervals with alkaline salts, hexamine, and had had several doses intravenously of mercurochrome-220 soluble solution, all without effect. After observation for several days, a mass was found in the left side. This was evacuated and a large amount of pus was obtained from a greatly enlarged renal pelvis. Following the operation the child improved for about ten days, then the high temperature returned and a second operation for better drainage became necessary. The surgeons considered seriously the removal of the kidney. Before this was done, however, cystoscopic examination revealed that there was no ureteral orifice of the right side but that the child probably had a greatly hypertrophied single kidney. Roentgen-ray examinations were practically negative. At the time of operation it was felt that the enlarged kidney was not of the horseshoe type. Following the second operation, the child made a satisfactory recovery, the renal function, as shown by the phenolphthalein and other tests, being almost normal. I speak of this case to emphasize that it is possible even in an infant to examine

the interior of the urinary bladder, and to emphasize that in this instance the information so obtained had saved the life of the child.

DR. HELMHOLZ: In addition to these fifteen cases, we have had one case of cord bladder, developing after injury. In one of the fifteen cases, the patient developed pyelitis at the age of 1 week. We could not make a cystoscopic examination at that time, but an examination made when the child was 10 months old showed that there were 2 ounces of residual urine and a definite cord bladder. I do feel that there is a definite group of chronic cases not associated with abnormality in the genito-urinary tract, as I have seen enough of these cases in which hexamine and ammonium chloride have been able to clear up infections that have existed anywhere from two to seven years.

In the interesting group of cases Dr. Abt brought forward, I am wondering how many belong to the cord bladder group. The history was suggestive in the first three cases, in which no obstruction was found for the enlargement in the ureters, and dysfunction of the bladder might have been the cause.

I have also looked up our other cases of malformations of the urinary tract. There were four cases of posterior urethral stricture, three cases of reduplication of the ureter with unilateral infection relieved by removal of the kidney. In one patient the ureter entered the bladder inside of the bladder sphincter. Nine cases showed a condition of dilated pyo-ureters, two on the left side and in the remaining on the right side. The exact cause was not determined. There was no obstruction and no evidence of any dysfunction of the bladder.

DR. ABT: What Dr. Helmholz said of the neurogenic origin of these cases is of great interest. It is also possible that at least one of our series was of this nature. On the other hand, when definite malformations such as double ureter or other anomalies exist, the cause must be considered congenital, and not due to spinal cord lesion.

I would like to emphasize the point brought out by Dr. Koplik. He mentioned that it is a severe technical procedure to inject opaque substances or otherwise manipulate the ureters in infants. That is undoubtedly true. Urologic examination should only be made after the ordinary methods of diagnosis and treatment have failed, but if in spite of proper treatment, symptoms persist for a long time, an investigation should be made employing urologic technic.

THE KETOGENIC DIET IN THE TREATMENT OF IDIOPATHIC EPILEPSY. Presented by DR. FRITZ B. TALBOT, DR. KENNETH METCALF (by invitation) and MARGARET MORIARTY, S.B. (by invitation), Boston.

Idiopathic epilepsy is taken to mean that type of epilepsy in which all physical, surgical, infectious and neurologic causes for the recurrent convulsions have been eliminated.

A small amount of evidence has appeared in the literature, principally the work of Jarloev (*Compt. rend. Soc. de biol.* **84**:156, 1921), Geyelin (*M. Rec.* **99**:1037, 1921, *Arch. Pediat.* **40**:480, 1923), and Dautrebrande (*J. A. M. A.* **86**:1229, 1926) which suggests that there is a relationship between the acid-base equilibrium of the body and the convulsive attacks, and that when the reaction of the body is more alkaline the attacks are more apt to occur. In 1921, the children's medical service of the Massachusetts General Hospital initiated a study of the treatment of idiopathic epilepsy. The first method of attack was by the fasting method recommended by Conklin of Battle Creek. Since that time twenty-three children have undergone therapeutic fasts for the treatment of their convulsive attacks. The last ten of these cases were studied chemically, and reports of eight of them appear in the papers by Hoeffel and Moriarty (*Am. J. Dis. Child.* **28**:16, 1924, and Shaw and Moriarty

(*Am. J. Dis. Child.* **28**:553, 1924). Almost without exception these children were free from convulsive attacks during the period of fasting in which there was a hypoglycemia, ketosis and slight acidosis. The attacks, however, returned sooner or later in all cases that could be followed.

It became clear that repeated fasting was not a practical procedure to carry out in the treatment of this condition, nor was it possible to maintain a ketosis between fasts. The method recommended by Peterman (*Am. J. Dis. Child.* **28**:28, 1924), of causing a ketosis by adjusting the diet so that the ketogenic factors in the diet outbalanced the antiketogenic factors, was instituted in the fall of 1924, and since that time thirty-two patients were referred to the epileptic clinic for this method of treatment. Twelve of these cases were found to be suitable for treatment, and have been under supervision for various lengths of time up to a year. The other twenty were unsuitable either because they lived too far away to report frequently enough, because they could not follow the diet, were feebleminded, or had physical causes for their convulsions.

It was found that blood changes, similar to those seen during fasting, resulted in the patient in whom a ketosis had been caused by diet. In both instances the blood sugar became reduced; there was a marked production of acetone and a lowering of the carbon dioxide combining power of the blood. This condition of ketosis could be maintained almost indefinitely if the diet was followed consistently. Large amounts of acetone were found in the blood and excreted in the urine over periods of weeks or months without causing any untoward symptoms in the patients. On the contrary, they seem to be more alert and less nervous. The general health of this group of children has been especially good; two children went through attacks of grip without any change in the diet. When carbohydrate foods were taken by any of the children the ketosis disappeared very rapidly.

It has been found necessary to have the ketogenic-antiketogenic ratio at least 3:1 before obtaining the best results. Seven of the twelve patients have been free from attacks from three to six and one-half months. Of these patients, five had grand mal and two had petit mal. The previous interval of attacks varied from four in the week to one attack every two months. These patients are thought to be definitely improved.

Three more patients are thought to be slightly improved. In one of them the attacks were reduced from 30 a week to 4 a week after one month of the diet. The second, from 18 a week to 6 a week after two weeks of the diet, and the third had had a grand mal attack every three weeks before instituting the diet and has had no attack for eight weeks. The other two clinic patients are unchanged. They continue to have attacks but break the diet frequently, losing the ketosis. One child in private practice, aged 15 years, who has been under treatment for seven months, has not improved to the same extent. The attacks are slightly less frequent and decidedly less severe under the diet.

These children are given 1 Gm. of protein per kilogram of their expected weight. The food intake and the urinary output of protein has been quantitated on 234 days. Most of this data were obtained on two patients, on one of whom these records were kept for four months, and the other for nine weeks. It was found that this amount of protein more than took care of the protein requirement for maintenance and growth, and in a rare instance when there was a nitrogenic deficit for a day or so.

The evidence given by Peterman and our own experience seems to indicate that in selected cases a ketogenic diet influences favorably the convulsive

attacks known as idiopathic epilepsy in young children. It is said to be not so efficient in the adult. It is difficult to decide whether the beneficial action which seems to occur is due to the acidosis, the hypoglycemia, or the ketosis per se. Studies are now under way in the attempt to differentiate these factors.

DISCUSSION

DR. SCHLOSS: It seems to be fairly well established that during starvation attacks of epilepsy are favorably influenced, and there seems to be evidence that in many instances the production of ketosis through fasting has the same effect. The mechanism by which ketogenic diets favorably influence epilepsy is a question of interest and naturally of the greatest importance.

As Dr. Talbot has brought out, the beneficial influence is not due to acidosis per se, since acidosis produced by ammonium chloride or by hydrochloric acid is without favorable influence. It is possible of course, that the favorable influence is due to the anesthetic effect of the acetone bodies. It is well known that acetone has a definite anesthetic effect, and occupies a position in activity midway between alcohol and ether. In the experimental animals, however, it requires from 3 to 5 per cent of acetone in the blood to exert an anesthetic effect, a quantity which is never approached in the blood of infants in ketosis. At the same time, it is possible that acetone formed directly in the tissues may have a more marked effect than acetone administered orally or parenterally.

If it is true that the efficacy of ketogenic diets lies in the anesthetic effect of the acetone substances, then this type of treatment is directly analogous to the use of sedative drugs and can hardly be expected to be of permanent value. The use of ketogenic diets in young children involves much difficulty owing to the huge amounts of fat which these children must ingest. In my experience, it is a matter of great difficulty to induce children to remain for any considerable period of time on diets of this kind.

DR. BARTLETT: I was interested in what Dr. Talbot said as I studied this subject last winter. The number of cases was much smaller, however. We have the feeling that children with a certain degree of mental deterioration show less promising results than the children whose mentality is much better. Of this I cannot be positive, but I just throw it out as a question. Also, the children with minor attacks seemed to respond more favorably. That this diet is valuable in certain types seems to be fairly clear. The continuation of the diet over long periods is difficult because of the unparalleled quantity of fat.

DR. LA FETRA: In connection with the length of time these diets can be continued, I wish to record a case in practice. Four years ago, a girl, aged 9 years, previously in perfect health, had major attacks occurring three or four times a day, then an interval for a week or so. I knew of Dr. Talbot's work and wanted the treatment carried out. I asked Dr. Geyelin of the Presbyterian Hospital to undertake the regulation of the diet, so the adequate result is due to his care. He started with the diet and the child in the first three months had intervals of fourteen to twenty-one days. She had no attacks during the fasting days, but she had attacks in the intervals. For about three years and six months she has been on the ketogenic diet which she takes with a perfectly normal relish. She has been entirely free from attacks during all that time. I asked Dr. Geyelin just before I came up in regard to his results with the ketogenic diet, and Dr. Geyelin found he had 23 per cent of complete relief, with absence of attacks for periods of three to six years. In cases of fasting

for less than two years, 15 per cent were greatly improved and the remainder were entirely unrelieved.

DR. HELMHOLZ: I have been greatly interested in Dr. Talbot's paper, because we have been working along the same lines, and our results are practically the same. We find that with a relationship of 1 Gm. carbohydrate to 4 Gm. of fat, acidosis is usually established, but it is rarely sufficient to produce a cessation of the attacks; a ratio of 1 to 5 or 6 is necessary. One gram of protein per kilogram seems amply sufficient for growth; if larger amounts of protein are used, it is difficult to produce ketosis. Vomiting was the only difficulty we had with the earlier patients in whom we attempted to establish ketosis too rapidly. In another type of epilepsy, seven cases following encephalitis, the diets seemed to be of some benefit; in three cases there was no change and in the other four there was no complete cessation of the attacks, but the interval between attacks was prolonged. Of sixty-six cases, twenty-one patients, or 32 per cent, were entirely free from symptoms for six months, which corresponds with Dr. La Fetra's figures from Dr. Geyelin. There was definite improvement in twenty-six, which is over one-third. In considering those who were improved, it must be said that in a number of them it was difficult to keep the child constantly in a state of ketosis. The children will manage to obtain candy, bread and other foods. There were nineteen flat failures when the diet was kept up long enough to indicate whether or not it was of value. We had other cases not in ketosis long enough to be included in this group. We found that in petit mal type of epilepsy, we had our best results. We have found further, that after these patients have been in ketosis for six months you can gradually relieve them from the severity of the diet and still keep them free from attacks. Some of the patients have been free from attacks for over three years now.

With regard to the difficulties of carrying out this diet, as mentioned by Dr. Schloss, we have had it in the highest degree. Our patients are under direct observation for only a short time, and after they leave we must take care of the diet by correspondence. We have to teach the mothers how to carry out our instructions in a short time, and to do this we have developed a manual which we have found to be of great assistance.

DR. CHARLES HENDEE SMITH: I should like to ask Dr. Talbot if he uses drugs in connection with this diet. It is well known that phenobarbital will diminish the attacks. It has seemed to me that by combining this drug with the diet, one can ease up on the diet or reinforce it when it does not work, and at the same time accomplish similar results.

DR. TALBOT: It is interesting to find that similar experiences have been seen in other clinics, and gives us encouragement to keep on working at the subject. Dr. Schloss spoke of the huge amounts of fat. They are huge amounts. It is what we call a 4 to 1 diet when the child is receiving 1,850 calories per day, 40 Gm. of protein, 186 Gm. of fat, which is a tremendous amount. The method used by Dr. Helmholz and Dr. Peterman in estimating the ketogenic ratio is not the same as ours. What they consider 6 to 1 diet is about the same as what we consider a 4 to 1 diet. It is difficult in some cases to get a child to take all the cream or fat necessary, and one of the tricks is to use different kinds of fat, olive oil, cod liver oil, bacon, butter and cream. In some instances the bacon fat is cooked in muffins. A clever dietitian works out various little tricks to get in fat. Giving acid to cut fat enables us to get in additional fat. We use a great deal of vinegar which is carbohydrate-free in salads. We had only one instance in which there was

any trouble in keeping the child's stomach settled for a short time. There was nausea on a 3 to 1 diet; now the child takes a 4 to 1 diet, which corresponds to Dr. Helmholz's 6 to 1 without symptoms.

There has been some difficulty in keeping the child on this diet, but when the parents have tried all other forms of treatment without benefit, they are usually prepared to go to any amount of trouble to carry out any plan which offers hope of recovery. The children who appreciate their handicap are also often willing and glad to cooperate. A curious thing I noticed is that despite the fact that children on this diet are usually constipated, the complexion, which before has been muddy, clears up and becomes clear. We have also noticed that the children become less nervous.

Dr. Bartlett speaks of mental deterioration. We have not been able to do anything with children with mental deterioration. One reason is that such a child will not cooperate, even if the parents are willing to cooperate. Our impression is that when the disease has progressed to mental deterioration it has gone too far for ketosis to be of any benefit, and unless we are forced to do so we do not accept cases of that type. We have been forced to treat one or two cases in which there was a physical basis for the epilepsy, and it is our impression that the diet is not so successful with this type of patient.

I would like to correct one impression that might have been obtained from Dr. La Fetra's discussion. In reference to Dr. Geyelin's results: Dr. La Fetra said that Dr. Geyelin had had 23 per cent of complete relief for from two to six years, but the earlier cases were fasted and were not on the ketogenic diet. Is that not the case?

DR. LA FETRA: Yes.

DR. TALBOT: Dr. Helmholz's statement about the great importance of not creating ketosis too rapidly is a very important factor. In cases in which ketosis has been brought about slowly there is no difficulty at all. My assistants in the hospital all feel, as Dr. Helmholz suggests and as Dr. Peterman said the other day, that the ingestion of sugar or carbohydrate in any form will bring on attacks.

In answer to Dr. Smith, in order to quantitate the results we have stopped giving phenobarbital. It is our impression that these children brighten up when in a condition of ketosis, and they fall back when they have no ketosis.

It is extraordinary to see how rapidly a small amount of sugar will correct a severe ketosis. In these children with hypoglycemia, a small amount of sugar will counteract the condition whether given by mouth or subcutaneously.

Book Reviews

THE METABOLISM OF CHILDREN DURING FEVER. PROF. DR. W. BIRK, Beihefte zum Jahrbuch für Kinderheilkunde, No. 9, 1926.

The monograph of 104 pages contains the results of the author's studies on the protein and mineral metabolism of infants during fever. In the first twenty-five pages, he reviews the meager literature. Following Naunyn, the older observers ascribe the rise in protein metabolism occurring in fever to a toxic destruction of protoplasm. In accord with Krehl, more recent observers attribute it to a disturbance of central nervous origin. Animal experiments have demonstrated the existence of regulating centers in the brain which control the total metabolism (body temperature) and also the metabolism of protein, fat and carbohydrate (the latter being known since the time of Claude Bernard). The author cites the rather unconvincing evidence for this conception, and concludes that the mechanism controlling protein metabolism is as follows: A parasympathetic center located in the midbrain retards the metabolism of protein. This center corresponds to that portion of the heat regulating center which lowers heat production. Similarly, a sympathetic center in the midbrain stimulates the metabolism of protein and corresponds to the sympathetic portion of the heat regulating center which raises the heat production. Finally, the liver contains protein depots analogous to its glycogen depots. Ordinarily with a normal temperature the parasympathetic center predominates, and sends inhibiting impulses to the liver by way of the vagus which holds the metabolism of protein in check. When fever results from stimulation of the sympathetic heat center, impulses pass to the liver by way of the sympathetics which accelerate the metabolism of protein. The mechanism is analogous to the mobilization and storage of glycogen in the liver resulting from sympathetic and parasympathetic stimuli respectively.

In the remaining pages, the author presents the results of eleven observations in five artificially fed infants, aged from 3 to 7 months: (1) The influence of different infections on the protein and mineral metabolism (Cl, Ca, Mg, P, Na, K); (2) the metabolic changes occurring in the incubation period of an infection, and (3) the persistence of these changes after subsidence of fever. He studied the infants during control periods and in the prefebrile, febrile and postfebrile stages of measles, chickenpox, nasopharyngitis and the induced fever of vaccination. Analyses of ingested food, stools and urine in experimental periods furnished data for calculating amounts and proportions of constituents retained. The diets throughout remained as constant as possible.

Alterations in the protein metabolism appeared in five out of the six infants in the incubation period preceding any loss of weight or rise of temperature. The changes are usually in the direction of a diminished nitrogen retention and increased nitrogen excretion. However, during this period there is occasionally an improved retention. The latter finding may only be explained on the beforementioned mechanism. In the fever period, the nitrogen retention fell in all the cases, the extent depending on the severity of the infection and the height and duration of fever. In the postfebrile period, the increased nitrogen excretion continued for some time in most instances. The fact that no compensatory rise in the nitrogen retention occurred in this period favors the conception of

protein depots rather than the source of nitrogen being from destroyed protoplasm.

Increased retention of chlorine during fever was manifest in nearly all observations. The results were variable during the incubation period. The presence of fever resulted in a reduction in the calcium retention in all infants. This finding may explain the appearance of symptoms in latent tetany during the course of an infection. The magnesium retention was also reduced in fever. In the majority of the infants, the phosphorus retention declined during the fever periods. However, in several instances the balance improved. Changes in the sodium and potassium metabolism were too variable to interpret.

The experiments seem to be carefully planned and the results clearly presented. In view of the comparatively few observations and the somewhat inconsistent results, it would appear that the author would perhaps have done better by a statement of the facts without any attempt at a theoretic interpretation of the mechanisms involved.

GASTRO-INTESTINAL INFECTIONS IN THE INFANT AND THE YOUNG CHILD. MONOGRAPH. By EUGENIO CIENFUEGOS, Santiago, Chile; Imp. Bellavista.

In a comprehensive monograph, this eminent South American Pediatrician discusses in detail the gastro-intestinal infections so prevalent in parts of South America and playing such an important rôle in the mortality figures of some of the large cities, notably Santiago.

In Chile, infectious intestinal disorders (ex infectione) are far more common than those due to purely food factors (ex alimentatione).

Among the different organisms which can cause these intestinal infections are mentioned ameba, dysentery bacilli, various coli bacilli, and other organisms producing diarrhea. Various clinical pictures may be produced, for example, septicemias without pronounced local phenomena or manifestation of enterocolitis or rectosigmoiditis. The symptoms of a pronounced toxicosis may predominate and eventually lead to the picture of athrepsia or decomposition. Again the picture may be that of an acidosis or of recurring intestinal infection.

The author points out that certain geographical and social conditions are big factors in the cause and development of these gastro-intestinal infections. He divides the infectious disorders of the infant as follows:

1. Infectious disorders with a specific lesion of the intestinal canal such as
   (*a*) Follicular, enterocolitis.
   (*b*) Rectosigmoiditis.
   (*c*) Typhoid fever.
   (*d*) Intestinal tuberculosis.
2. Infectious disorders without any determined specific lesion:
   (*a*) Slight infections and enterocatarrh of the intestine.
   (*b*) Chronic recurring infection.

The author believes that in his community three principal factors can cause enterocolitis.

1. Protozoa — particularly ameba. This infection probably accounts for about 10 per cent of all cases.

2. The presence of dysentery bacilli.

3. Ordinarily harmless organisms generally classed under the groups of anaerobes. Under certain conditions these organisms can take on harmful characteristics.

In addition to these principal factors, exogenous infections may produce enterocolitis, for example, focal infections from the throat. Most of the enterocolitis cases are observed during the summer. Heat is a big factor. The author regards it particularly so in Chile, where in contrast to the extreme heat of mid-day, the evening and nights are chilly and cold.

Very frequent and fetid stools are a bad omen and warrant a grave prognosis. The same is true if there are other evidences of general systemic infection and pronounced intoxication. In the acute cases, pyelitis or pyelonephritis are fairly common complications. In the chronic case bronchopneumonia is the dangerous element.

The treatment varies according to the age of the patient. Breast feeding is the best procedure for the very young infant. As a substitute, the author's choice is buttermilk with or without carbohydrate additions or albumin milk with dextrimaltose added. He does not entirely endorse the farinaceous feeding advocated by Combe.

Troublesome vomiting is controlled by gavage and atropine. Other medication depends on the causal agent. If the infection is of amebic origin, the author uses emetine in the dosage of 0.02 Gm. given subcutaneously once daily. If this treatment fails, arsenic or the tartrate of bismuth may succeed. The author has had excellent results in bacillary dysentery with the polyvalent antidysentery serum of Hoechst. It is effective in both the acute and chronic cases.

The use of mercurial preparations is condemned, also high colonic flushings except in very chronic cases. In these 2 per cent solutions of tannin or 0.5 per cent silver nitrate solutions are often useful.

Rectosigmoiditis is generally a sequence of an enterocolitis. Prolapse of the rectum is often a rebellious complication. It is most commonly seen in infants with defective constitution and with pronounced neuropathic taint.

The author particularly recommends parenteral protein therapy in the form of injections of foreign proteins into the perianal mucosa. If the lesion in the colon is very distant or is in the rectosigmoid region, neither the quality nor the quantity of the food should be changed much from the normal. Subalimentation is dangerous and favors rectal prolapse.

In addition to the detailed discussion of enterocolitis, the author briefly discusses other gastro-intestinal infections such as typhoid fever, acute intestinal infections without specific lesion in the intestinal canal, and gastro-intestinal infections due entirely to extra-alimentary causes.

For the chronic recurring intestinal infections caused principally by anaerobes, and characterized by both general symptoms and local symptoms in the gastro-intestinal tract, the author recommends the autoenterovaccine therapy used so successfully by Julio Schwarzenberg. These vaccines are preferably given hypodermically, with an initial dosage of 5 to 10 million germs every other day, increasing this dosage steadily until 30 to 100 million have been reached.

This monograph is by far the most exhaustive treatise on the subject of gastro-intestinal infections which has appeared in the South American pediatric literature of recent years.

DIAGNOSTISCHE UND THERAPEUTISCHE IRRTÜMER UND DEREN VERHÜTUNG; KINDERHEILKUNDE, J. SCHWALBE, ZWEITES HEFT, KRANKHEITEN DES SAUGLINGSALTERS. By F. MEYER. Pp. 156. Price, $1.15. 1924: Georg Thieme.

L. F. Meyer devotes 156 pages to the diagnostic and therapeutic errors and their prevention in the diseases of infancy. The title is somewhat misleading,

the subtitles giving a better idea of the scope of the work, "Diagnostic and Therapeutic Errors in Diseases of the New-Born," and "Errors in the Physiology and Pathology of Nutrition." The little volume is written in the author's usual interesting manner. In the introduction, he quotes an old physician, "The true diagnostician and therapeutist is the physician at the bedside. What he sees and does, does not fit in any system and can only rarely be laid down in writing. All our teachings to observe patients obtained from books and in the lecture room can only be general." The "experienced" physician is much emphasized in the book, and to a certain extent justly, but, particularly in the field of therapeutics, human frailty can play the very dickens with that "experience." Just glance at the therapy of the masters in the history of medicine. What happened to such "experienced" observers can and certainly does happen every day to the best of us. Unfortunately, many diagnostic and therapeutic observations are laid down in writing with all the force of authoritative experience, when even rather crude measuring could have given better information. Indeed, we take it, the insufficiency of our unaided senses is responsible to a great extent for the necessity of the work of which this volume forms a part.

Not so many years ago, the dangers of overfeeding were strongly emphasized; now the ill effects of insufficient feeding are stressed particularly. In the treatment of the serious disorders of nutrition, we miss the blood transfusions, which are also of great help in the preparation of some cases of pyloric stenosis for operation. In cases of pyloric stenosis the possibilities of thick cereal feedings are perhaps not sufficiently recognized. Lactic acid milk should find a place at least among the therapeutic foods. An effort is made to combine a clinical with an etiologic classification of the disorders of nutrition, a classification which appears quite serviceable. Among the constitutional factors of nutritional disturbances of the breast fed infant, a hyperexcitability of the nervous system is given, which is further defined as a vegetative neurosis. It must be kept in mind that the foundations for the theory of the vegetative neurosis are very weak.